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Epidemiology and the bio-statistical theory of disease: a challenging perspective

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Abstract Christopher Boorse's bio-statistical theory (BST) of health and disease argues that the central discipline on which theoretical medicine relies is physiology. His theory has been much discussed but little has been said about its focus on physiology or, conversely, about the role that other biomedical disciplines may play in establishing a theoretical concept of health. Since at least the 1950s, epidemiology has gained in strength and legitimacy as an independent medical science that contributes to our knowledge of health and disease. Indeed, it not only provides important information about disease distribution and aetiology, but the risk-factor approach it employs seems to challenge BST's binary conception of health and disease. The objective of the article is to show, firstly, how important information deriving from descriptive and analytical epidemiology forms part of our contemporary medical concepts of health and disease, and secondly, that these elements are not taken into account by BST in a satisfactory way. The article's central contention, therefore, is that if the project of defining the theoretical concept of health is to be maintained, more importance should be accorded to the contribution made by epidemiology—alongside physiology—in defining health.

Keywords Boorse · Disease · Bio-statistical theory · Risk-factor · Epidemiology · Normality

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Introduction

Christopher Boorse's bio-statistical theory (BST) of health, which was first defended in a series of papers published between 1975 and 1977 [1–3], can still be considered the main and strongest naturalist view of health. Nevertheless, the meaning of 'naturalist' in this context is not very clear. At minimum, it could be said that Boorse's account aims to *describe* the theoretical and value-free concept of health as used in the fundamental theory of medicine, i.e., in Boorse's view, physiology. Other distinct practical concepts of health are required for clinical and social approaches, which are inevitably evaluative. Those clinical or social concepts (e.g., diagnostic abnormality that is a 'clinically apparent pathological state') are constructed by adding evaluative criteria to the theoretical concept, for 'diagnostic normality is already value-laden because, among other reasons, what diagnostic tests are justified depends on risk, cost, and benefit' [4, p. 12]. To describe the theoretical concept of disease, i.e., the pathologist's concept, Boorse uses the method of conceptual analysis. In his view, the theoretical concept rests on a close articulation of three components which are thus considered to be used by physiology to conceptualise health: physiological function, reference class, and statistical subnormality [4]. A *physiological function* is defined as a causal contribution to physiological goals, i.e., to the survival and reproduction of an organism, and is relative to a 'reference class' smaller than species, e.g., an age group of a sex of a species. The reference class is defined as 'a natural class of organisms of uniform functional design' [3, p. 562]. The normal level of functioning is *typical*, i.e., 'at *efficiency* levels within or above some chosen central region of their population distribution' (italics added). 'Functioning' in Boorse's view thus includes the notion of 'efficiency', and 'typical' here means prevalent: the distinction between the normal and the pathological relies heavily on the concept of *statistical normality* or prevalence. Pathology, then, consists in statistically subnormal functional efficiency, hence, Boorse's definition of disease: 'A disease is a type of internal state which is … an impairment of normal functional ability, i.e., a reduction of one or more functional abilities below typical efficiency' [3]. Health, by contrast, is the absence of disease.

Boorse's definition has been much discussed and several criticisms have been put forward, in particular of each of the three main components that together make up his definition of health.[1] It is often concluded that, in each case, the naturalist aspect of the definition fails since evaluative considerations ultimately prove to have been assumed [6–9]. But little has been said about the relevance of Boorse's exclusive focus on physiology, or about the contributions that various other biomedical disciplines could or should make to an analysis and description of the medical concept of health. With this in mind, it is interesting to note that, at least since the 1970s, what is called 'modern epidemiology' or 'risk-factor epidemiology' has gained in both strength and legitimacy, and is now considered a significant contributor to the construction of knowledge about health and disease in medical science. Modern epidemiology does not merely study the health distribution in

[1] For a synthesis and for Boorse's answers, see [4]. See also his recent 'Second Rebuttal on Health' [5].

human populations by statistical means but also studies inter-individual and inter-group variability, making comparisons and drawing inferences from these comparisons.[2] Recent philosophical analyses have supported the idea that epidemiology delivers proper explanations of health phenomena which are not reducible to physiological explanations.[3]

In this article, I confront BST with the findings of epidemiology regarding health and disease, the aim being to understand better the role this discipline plays—alongside physiology—in describing and explaining these phenomena. Sympathetic to Boorse's project of defining the medical concept of health, Maël Lemoine and I have shown elsewhere [14] that a central issue of concern is BST's assumption of the uniqueness and centrality of physiology in defining theoretical health: other medical disciplines, we think, also play an important role and need to be taken into account if a viable definition of the medical concept of health is to be articulated. The purpose of the present article is to show that important information produced in the field of epidemiology forms part of the contemporary medical conception of health and disease and that these elements are not currently taken into account by BST in a satisfactory way. My contention is that, if the project of defining the theoretical concept of health is to be maintained, more importance should be accorded to the contribution made by epidemiology. I further argue that this approach requires us to undertake more than a simple modification or reinterpretation of BST, for it also calls for a new way of arriving at a naturalist account of health.

In the first section, I examine two ways in which epidemiological findings challenge BST. In so doing, I present various ways in which epidemiology contributes to our knowledge of health and disease. First, I focus on the so-called 'epidemiological transition' revealed by the morbidity and mortality studies of descriptive epidemiology. I show that the high prevalence of chronic diseases and the evolution of the population distribution of disease seriously call into question both the concept of 'statistical subnormality' and the concept of 'reference class' as used by BST to delimit the normal and the pathological. Second, I show how analytical epidemiology (or risk-factor epidemiology) raises difficulties for the binary classification of health phenomena (the normal and the pathological as mutually exclusive categories) defended by BST and tends instead to favour a continuous account.

[2] It could be objected that, whereas epidemiology concerns the health status of *populations*, BST aims to define *individual* health. One possible response to this objection is to say not only that population health impacts on individual health but also that the role of 'modern epidemiology' cannot any more be limited to public health: 'risk-factor epidemiology' now provides important information for individual health that is used in medicine [10, 11].

[3] Alex Broadbent has argued that epidemiology has a proper explanatory role which relies on the contrastive model of explanation [12]. Contrastive explanation of disease consists in citing causes that are present in cases of disease and absent otherwise. According to Broadbent, epidemiology may thus suggest new kinds of disease, as in the case of, say, obesity, or as regards various risk factors (see [12, p. 146]), and can also help to redefine diseases thanks to its analysis of causation (see [12, p. 158]). See also Federica Russo who has examined what she calls 'variational' epistemology [13]. I also defended the characterization of the explanatory role of epidemiology as the one that is attached to 'population thinking' as described by Elliott Sober [10].

In the second section, I critically examine some possible answers to these objections, drawing both on Boorse's formulation of BST and on recent amendments or improvements proposed by some of its contemporary advocates, such as Peter Schwartz and Daniel Hausman. My aim here is to examine whether and to what extent BST could integrate some of these epidemiological findings without having to consider that epidemiology has any fundamental contributions to make to the definition of the theoretical concept of health. Concerning the first challenge of the first section, it could be argued that BST's concept of health is age-relative and thus can easily account for the recent prevalence of chronic or degenerative diseases, in which case there would exist what is called 'normal aging'. About the second, it could be maintained that the risk-factor approach only concerns preventive medicine and 'instrumental health' (in Boorse's terms) but not curative medicine and 'intrinsic health'. As I will show, however, these interpretations of BST and the responses they make possible are both insufficient and limited.

In the third section, I suggest that by considering epidemiology's fundamental contribution to theoretical knowledge of health phenomena, some difficulties encountered by BST can be resolved, or at least better understood. I further argue that taking epidemiology into account also requires renouncing some of BST's central components. In so doing, I sketch out epidemiology's potential contributions to the medical definition of health, arguing that this discipline is complementary to physiology in its approach to health and disease phenomena. More analysis, however, would need to be carried out in order to determine the exact contribution of epidemiology to the definition of a theoretical concept of health and thus also to develop a better and more precise definition of health and disease.

How epidemiology challenges BST

This section examines two main ways in which epidemiological findings could be seen to present a challenge to BST. The first concerns the epidemiological transition brought to light by descriptive epidemiology. The second concerns the findings of etiological research in the context of analytical epidemiology. The issues raised for BST are not necessarily new—the first in particular—but I will show how the epidemiological perspective sheds new light on them. My aim here is also to begin bringing attention to the specific contribution of epidemiology to knowledge about health and disease.

The epidemiological transition: common chronic diseases and dynamicity of health distribution

One of the tasks of epidemiology is descriptive: it describes the distribution of health and disease phenomena by characteristics related to *time*, *place*, and *persons*, using statistical data. During the period 1920–1950, several health and morbidity studies led by epidemiologists revealed an important shift in the morbidity status of the populations of certain developed countries. This shift, which was later theorized in demography and medical geography by Abdel Omran as the 'epidemiological

transition', accounts for the replacement over time of infectious diseases by chronic diseases [15]. Omran analyzes and describes three phases in the evolution and decline of mortality in human populations. The final phase, during which chronic diseases replace infection as the primary cause of death, is called 'the age of degenerative and Man-Made Diseases'.[4] Ever since this 'epidemiological transition', several chronic conditions, in particular, cancer and cardiovascular diseases, have become common and appear as almost 'typical' in the reference classes of seniors, and even in some other reference classes of adults. Today, some are frequent in over 20% of the population distribution of the older reference classes. These include atherosclerosis, hypertension, osteoporosis, and prostate cancer. Yet, medical usage counts them as diseases.

Two main implications of this transition are of interest with respect to BST: the chronic disease epidemic and the historical evolution of disease distribution. The first of these appears as a problem for the concept of statistical normality and, more specifically, the well-recognized 'universal disease problem' that Boorse himself regards as an anomaly [3]. This problem has recently been further developed in what Peter Schwartz called the 'common disease problem' [16], i.e., the problem of diseases that afflict a considerable minority of a population. For example, a quarter of all men over the age of 70 suffer from urinary dysfunction due to benign prostate hypertrophy. This problem seriously questions the importance given to the idea that the line between the normal and pathological functioning is statistical (in the sense of prevalence). The chronic nature of current prevalent diseases in developed societies raises another problem for BST, one that is not pointed out by Schwartz. These diseases have a long, progressive, and incremental development, as well as multifactorial origins. Yet, in focusing on the physiological dysfunction, i.e., the underlying pathology, it could be said that in causal terms, BST only allows proximate causes to enter into its definition of disease. As I will show in the next subsection on risk-factor epidemiology, in order to understand and characterise these 'modern' chronic diseases, the medical sciences have had to look beyond proximate or immediate causes (the underlying pathology) in order to investigate the aetiology, i.e., those internal or external causes that are more distal or temporally remote. It could thus be asked if BST is as relevant for chronic diseases as it is for acute diseases.

The second implication of the epidemiological transition—the historical evolution of disease distribution—reinforces, albeit in a different way, a problem already pointed out by J. David Guerrero [8]. Guerrero has shown that what he calls the 'Cambridge-change', a change in what is counted as disease, is a problem for BST. This expression refers to the fact that an individual's health status can change, not because of any internal physiological change (as required by BST), but merely because of a change in the rest of his or her reference class. Imagine, Guerrero says, that George's heart had average blood-pumping ability, but that the rest of current humanity instantly acquired the cardiac fitness of Lance Armstrong, then George would, in this context, become instantly diseased. Such an example stresses the fact

[4] The main aspects of the last phase is the major reduction of infant mortality rates and the extension of average life expectancy, which, coupled with declines in fertility rates, induce or reflect the transition to chronic diseases. This transition occurs in developing countries as they undergo the process of modernisation and develop modern healthcare.

that in BST, the definition of health and disease is highly dependent on their distribution in the chosen reference class. In BST, the normal level of functioning should be typical, i.e., 'at efficiency levels within or above some chosen central region of their population distribution' [3, p. 559]. BST thus entails that what was normal yesterday could prove to be pathological tomorrow. According to Guerrero, the possibility of such a change renders BST 'theoretically dubious' [8]. Nevertheless, it should also be noted that Guerrero uses a hypothetical example in which change is very rapid, and which, as such, is not very realistic. As I will show in the next section, the progressive change characteristic of the epidemiological transition raises deeper difficulties that are not easily answered. The epidemiological transition reveals the dynamic characteristic of the health and disease distribution in human populations. In so doing, it seriously questions the relevance of BST's concept of a *stable* and *natural* human design ('a natural class of organisms of uniform functional design') to which health functional statements are relative: should we and could we consider, as BST seems to do, that the reference classes used for health judgments are the same both before and after the epidemiological transition?

To sum up, even if *descriptive epidemiology* is considered not to directly contribute to *defining* disease, since it counts conditions already categorized as pathological, it contributes significant information about the evolution of its population distribution. Since such a distribution plays a role in BST for the demarcation of the normal and the pathological and, at least in some way, in the definition of the reference class, this information should be consistent with BST. Yet, as shown in this section, information delivered by descriptive epidemiology raises serious questions about BST's concepts of statistical normality and of stable and natural reference classes.

The risk approach and the normal-pathological distinction

Another challenge to BST comes from the fact that epidemiology now plays a central role in identifying the 'risk factors' of diseases, enriching and modifying understanding of their causality and nature, as well as the relation between the normal and the pathological. What is conventionally called 'modern epidemiology' came into being primarily in the United States and England in the decades following the Second World War. In the context of the 'epidemiological transition', this discipline broadened its scope to cover both chronic and infectious diseases, and some important methodological shifts led to the emergence of what could be called 'risk-factor epidemiology', which was in turn accompanied by a new form of preventive medicine. Epidemiology now plays an important role in the investigation of disease aetiology within etiological studies (mainly cohort and case–control studies[5]) and in modelling disease multifactoriality. In measuring the correlation between two variables (exposures and outcomes), aetiological studies make possible the identification of the risk factors of disease and the analytical role of

[5] A cohort study is a study following a population of people over an extended period of time and recording exposures of interest and outcomes of interest. It is generally prospective, but it can also use historical data. A case-control study is a study comparing how often an exposure of interest occurs in empirical cases, as compared to controls.

epidemiology is no longer confined to the investigation of the environmental and external factors of disease. Cohort studies conducted in the 1950s through 1960s—such as the famous Framingham Heart Study,[6] a cardiovascular epidemiological study that played a central role in the emergence of the risk-factor approach to disease [11, 17]—confirmed what had already been shown by health assurance statistics. They showed that some variations of a physiological characteristic (e.g., blood cholesterol, blood pressure) that are within the statistical 'normal range' of their population distribution are associated with an increased risk of morbidity and mortality (cardiovascular disease). It should be noted that, at that time, very little was known about the pathology of cardiovascular diseases. Thanks to these new types of studies, various characteristics, including not only environmental variables but also physiological variables, habits, lifestyle, and so on, have been conceptualized as 'risk factors' for diseases. Epidemiological knowledge of disease aetiology has proved to be very important in understanding these chronic diseases (cancer and cardiovascular disease), which now appear as the complex result of intricate degenerative processes and environmental (social as much as natural) influences of both distal and proximate origin. These risk factors have since become new targets for medicine oriented towards people considered *at risk of disease* rather than *normal* or *healthy*. A third category complicating the binary distinction between health and disease thus seems to have appeared; unless, that is, the risk-factor approach favours instead a more continuous account of health and disease.

Risk-factor epidemiology thus reveals further problems for the bio-statistical demarcation between the normal and the pathological. Some statistically normal characteristics or traits have proved to be indicative of risk of disease and some of them are now categorized as pathological, or at least as what Peter Schwartz has called 'risk-based diseases' [18]. The very notion of risk challenges binary and categorical ways of thinking, and thus, also an idea that lies at the core of BST: health and disease, the normal and the pathological, are mutually exclusive (health is the 'absence of disease'). 'Risk-based diseases', such as the paradigmatic cases of hypertension and hypercholesterolemia (as used as an indicator of the atherosclerosis process), form a continuum with normal states and thus have an equivocal and unclear status, located somewhere between the normal and the pathological. The difficulties encountered in the definition of the normal level of blood pressure, i.e., in drawing the demarcation line between normotension and hypertension, are paradigmatic of this new equivocal status, which is in large part the result of modern epidemiology's risk approach [11, 19]. In contemporary medical practice, the limit of normality for such a variable does not rely on the normal range, i.e., the population distribution of statistical parameters of blood pressure levels. Rather, it relies on mortality increasing linearly with increased blood pressure, as well as on other economic and therapeutic parameters. In this context, then, it would seem that there are no natural thresholds between risk and absence of risk. Far from being natural, the distinction between the normal and the pathological is henceforth the result of a decision taken on the basis of multiple evaluative parameters including

[6] The Framingham Heart Study, a prospective cohort study on cardiovascular disease carried out since 1948, is often seen as the paradigmatic model of such a design and method.

therapeutic benefits, the modifiability of the risk in question, interferences with the duration of a worthwhile life, as well as public and economic health aspects. Statistical normality, then, is no longer the criteria of normality for these physiological characteristics and the very idea of a natural and objective demarcation line (even a vague one), which is so central to BST, becomes meaningless. This conclusion seems to encourage the view that health judgments are fundamentally comparative, and thus, that health is what Andrew Schroeder has recently called a comparativist concept [20].

Epidemiology, which relies heavily on statistics, thus seems to imply that the statistical concept of normality should be abandoned. Analytical epidemiology fosters a different view of the non-pathological or normal, and the risk approach to disease calls into question BST's traditional way of thinking about health and disease as exhaustive and mutually exclusive states. Either epidemiology favours a comparativist concept of health, according to which there is a continuum from perfect and ideal health to disease, with in-between states 'at risk of disease', or if a binary way of thinking (normal vs. pathological) is maintained, it extends the pathological domain and correlatively restricts the concept of health by integrating into its meaning the probability of remaining healthy in the future (or the reverse). Thomas Royle Dawber, one of the principal architects of the Framingham Heart Study, insists on the changes in the concept of normality that result from modern epidemiology and argues for the first of these two alternatives. In his own words, 'Better knowledge of the natural history of the atherosclerotic process has led to a different concept of normality: that the normal person is one who not only has no disease but also is unlikely to develop it. At the extreme of this normality is the ideal individual who will never develop disease. The importance of this changing definition is best illustrated by the concept of risk factors as they pertain to the development of atherosclerotic disease' [21, p. 223].

Dawber's approach raises some novel issues, for it seems to open the door to an unlimited broadening of the pathological domain and to the medicalisation of normal life. Moreover, it is not yet clear whether epidemiology serves to define the pathological or only the factors that tend to produce the pathological. In any case, current medicine is increasingly confronted with the uncertain status of the patient 'at risk of disease'. At this point, it could be said that analytical epidemiology served to alert us to variables that physiology did not previously consider as dysfunctional, while at the same time stressing the fact that in the context of certain chronic diseases, there appears to be no natural theoretical demarcation between the normal and the pathological, but only different levels of functioning.

To sum up, it could be said at this stage that descriptive epidemiology and analytical epidemiology call the following into question: the relevance of the concept of statistical normality in demarcating health and disease; the binary view of health and disease in the context of chronic diseases; and the concept of the reference class as defined by BST. In the following section, I examine whether and to what extent some possible answers to these objections could be found both in BST itself and also in recent analyses and defences of this theory. These answers could potentially integrate the results of epidemiology without thereby leading to

the conclusion that epidemiology contributes—alongside physiology—to the definition of health and disease.

A critical examination of possible answers

How typical are chronic diseases for seniors?

I now consider how Boorse deals with the 'anomaly' of what he calls 'universal diseases'. For Boorse, only *typical* universal diseases are problematic. His examples include lung irritation and atherosclerosis. Epidemics of contagious disease, whose course is temporary and rapid, are excluded since they cannot be considered as typical of a reference class, defined on the basis of current and past populations as a reasonable time-slice of the species. To help with this anomaly, and without referring in any way to chronic forms of disease, Boorse added an environmental clause to his definition, by which a disease could also be 'a limitation on functional ability *caused by environmental agents*' [3] (emphasis added).

However, this environmental clause is highly problematic. It requires a very questionable distinction between internal and external causes of disease, as well as the difficult definition of what is a 'normal environment'. As noted above, 'modern chronic diseases' appear to be influenced by *social* (Omran's 'man-made diseases') as well as *natural* environments and depend on external or environmental factors no less than internal ones, which might be physiological or genetic. It is increasingly difficult, then, to draw a distinction between social and natural factors and between external and internal conditions. The criticisms concerning the difficult distinction between internal and external causes of disease led Boorse, in his 1997 article, 'Rebuttal on Health', finally to abandon the clause, considering that only 'a small part of a class [universal diseases] which is itself an infinitesimal part of the field [medically recognized disease]' is concerned [4]. However, although this is indeed a minor part of the pathological, it still represents a large number of people and this solution gives rise to a gap between BST and contemporary uses of the concept of disease. Furthermore, Boorse eventually adopts a prescriptive and stipulative approach to the definition—rather than a strictly descriptive one—suggesting that 'medicine should not recognize these universal diseases after all'.

Moreover, this clause—that disease could also be 'a limitation on functional ability caused by environmental agents'—is only relevant for diseases such as lung irritation. Typical or common diseases still exist—such as atherosclerosis—for which internal factors play a major role. Here again, Boorse adopts a stipulative point of view by insisting on the age-relativity of the physiological norms. To him, ageing is a normal condition and 'the puzzle is why old age is not always seen as a stage with its own statistical norms of healthy functioning' [3]. It follows that to be strictly faithful to the theoretical view of function and species design in physiology, physicians should consider only 'premature, or age-excessive, atherosclerosis' as pathological [4]. From this point of view, atherosclerosis—like any cumulative process partially due to normal ageing and caused from within—should be placed within the normal range of health parameters for the elderly.

But firstly, contemporary medicine considers that typical levels of atherosclerosis and hypertension in old age are pathological, and generally chooses not to count age as relevant after adulthood. The suggested solution thus increases the gap between BST and contemporary medicine. To solve the 'common disease' problem, Peter Schwartz rejects the idea that the line between normal and pathological functioning is statistical: even if prevalence matters, this line depends also on an evaluation of the 'negative consequences' of functional failure with respect to standard activities [16]. Schwartz's notion of 'negative consequences' is, however, rather vague; he did not really deliver details on it. Moreover, I will show below that this notion neglects the fact that statistical normality in BST concerns the level of *efficiency* of a function and that this functional efficiency already includes, at least in a certain way, an evaluation of certain *consequences* of the level of functioning.

Secondly, Boorse's insistence on the age-relativity of physiological norms, including the case of seniors, highlights and reinforces how problematic it is to suppose that the definition of the appropriate reference classes (portions of a species) for health judgments is objective. It should be recalled that, in Boorse's view, this objectivity relies on an *empirical* delimitation of 'ideal types of organisms'. The species or, more particularly, the 'species design' (i.e., 'the typical hierarchy of interlocking functional systems that supports the life of organisms of that type'), in Boorse's words, is empirically abstracted 'from individual differences or disease by *averaging* over a sufficiently large sample of the population. The species design that emerges is an *empirical ideal*…' [3, p. 557] (emphasis added). As there is a wide variety of functioning within the human species with regard to sex, age, and probably race, Boorse considers that physiology and medicine use reference classes smaller than species and that they are relative to age, sex, and race. The reference classes for heath judgments are thus defined as a class of people that displays a *specific* degree of balance between uniformity and heterogeneity of the functional human design that is *empirically* observed in a population. But what determines this specific level is not very clear. Why focus on age, sex, and race, rather than not being blind or having pneumonia? Should we distinguish adults and old people, i.e., should we count age as relevant after adulthood? What is the population (healthy and diseased? current? past?) over which 'averaging' is done? There seem to be some inevitably arbitrary, or at least value-laden, aspects to the delimitation and division of these reference classes.

Several authors have addressed this problem of constituting an objective reference class. Kingma [7] has clearly shown that nothing in nature empirically or objectively dictates the use of the reference classes Boorse proposes. Moreover, as Lemoine and I have shown elsewhere [14], physiology cannot itself determine what reference classes should be; at the very least, it should be conceded that the concepts of 'sample' and of 'averaging' are statistical in nature, and that the expression 'reference class' is rarely seen in physiology. Even if this notion is presupposed in physiology, it cannot be said to have emerged from physiology. Lemoine and I have further shown that it is questionable to claim that clearly defined reference classes are *necessary* to physiology: if the description offered by BST is supposed to capture the content of physiological textbooks, these same textbooks do not appear to describe the function in one reference class, say, elderly women, but instead,

describe and explain specific mechanisms and process of specific sorts that are not necessarily relevant candidates for characterising a reference class (e.g., living in high altitude). Idealisation in this field, as already shown by Wachbroit, is not statistical but rather 'theoretical', i.e., normal here means 'canonical' rather than 'frequent' [22].

To sum up, a major part of the answer to the objection of the problem of the frequency of chronic diseases for seniors relies on the definition of the reference classes, yet, contrary to Boorse's view, those reference classes cannot be objectively defined. Moreover, in relying on this concept, Boorse goes beyond the limits of physiology, though without explicitly recognizing that he has done so.

Dynamicity of statistical norms and the time-slice of the reference class

In responding to the 'Cambridge-change' objection, Boorse wrote that the theoretical possibility of a change in the species-typical functional capacity creates no conflict with BST[7] and is even an idea basic to scientific medicine. It is, however, extremely unlikely, he thinks, particularly when one considers that he includes a 'reasonable time-slice of the species' into the reference class, an important aspect that excludes the possibility of any instant change. But, while I agree with Boorse that this change does not create an internal conflict, I maintain that BST is currently ill-equipped to take account of a change in morbidity of the sort one observes in the epidemiological transition. Here again, the problem concerns the definition of the reference class and, more specifically, the problem of the *length of its time-slice*: what is a 'reasonable' time-slice? Boorse's answer is not only unclear but also lacks precision. He originally spoke of 'including "millennia" of the species history' [3], and later added that contemporary Western civilization is 'barely an eye-blink in the history of man' [4]. These remarks are in line with his view that physiology should be distinguished from evolutionary biology as far as medicine is concerned: 'Medicine does not regard failure to be in the evolutionary vanguard as a disease' [3]. But in his 'Rebuttal on Function', replying to Neander's criticism against the vagueness of the time-slice, he uses a negative formulation: 'any time-slice shorter than a lifetime or two seems too short for the very idea of species-typical functional design' [23, p. 99]. So, one can only conclude that the time-slice is between two lifetimes and millennia.

But then what about changes such as epidemiological transition? How can they be articulated with Boorse's notion of a reasonable time-slice? And can BST still claim it endorses the methodology of analysing and describing existing medical concepts if conditions such as atherosclerosis, hypertension, prostate cancer, obesity, osteoporosis, and so on, all of which are frequent in certain reference classes, do not fit BST's definition of disease, even though they are more and more viewed as diseases by medicine? At the very least, theoretical medicine and physiology cannot ignore epidemiological changes in human morbidity and in

[7] As Boorse points out, 'What is judged health or disease is still an internal functional capacity of the individual. What has change is only species-typical functional capacity—the benchmark for whether the individual capacity is healthy or not' [5, p. 715]. Thus, health is still an internal capacity, but it could be that its status changes without the internal capacity itself having changed.

human longevity, such as the epidemiological transition begun in the 1920s and 1930s in more developed countries. Thus, far from supporting the idea of a stable and natural human functional design, descriptive epidemiology reveals the importance of historical evolution of health phenomena at the population level and brings to light a crucial issue: the relevant time-slice extension of the reference class. While I approve of the difference between physiology and evolutionary biology as far as time-scale is concerned, it seems to me that a shorter population time-slice to which our theoretical health judgments are relative would better fit contemporary medicine.

Risk-based diseases: an erroneous use of the term 'disease'?

One possible answer to the uncertain status of risk factors that does not run the risk of conflating the normal and the pathological but preserves, instead, a binary way of thinking about health and disease is to understand the findings of risk-factor epidemiology as contributing not to the *definition* of the pathological but only its *aetiology* (i.e., its more distal and remote causes). Boorse himself maintains just such a demarcation between the category of 'risk factor' and the category of 'disease', one that runs parallel to the distinction between 'causation of disease' and 'disease (itself)' as well as to the distinction between preventive medicine and curative medicine. As noted above, in epidemiology, 'risk factor' can refer to a habit (e.g., smoking) or an environment (e.g., a stressful environment). The environment and the habit could be bad and produce disease without being themselves 'pathological'. For Boorse, it is clear enough that the expression 'risk factor' refers here to 'items that produce poor health, not exemplify it' [3, p. 553]. In the case of risk factors referring to *internal states*, i.e., 'dispositions to become diseased under certain conditions', the distinction between the disease and its risk factors, or in other words, between 'what a disease is' and 'what tends to produce disease', also rely on the distinction between a factor of a disease and the disease itself.

On this view, for an individual to have a risk factor does not mean he is not healthy. Boorse's dichotomous account of health and disease, i.e., his analysis of health as the absence of disease, is thus respected. The risk variation in *health* is nevertheless taken into account in BST thanks to the introduction of a distinction drawn within the category of health: the distinction between 'instrumental health' and 'intrinsic health' [3, p. 553]. For an individual, having (internal) risk factors for disease is compatible with intrinsic health, but some risk variations can make a difference in instrumental health without being assimilated to a disease. Two individuals will have equal intrinsic health, but one, the non-smoker, could be *instrumentally* healthier than the smoker. Recognising and identifying these factors of disease does not change our way of seeing the demarcation between health and disease. It only introduces differences inside the concept of health. From this perspective, epidemiology simply delivers important information for preventive medicine and what Boorse calls 'instrumental health', a subcategory of theoretical health, but not for curative medicine and intrinsic health. Boorse's solution is therefore the exact opposite of Dawber's (first section above): it integrates risk factors into the category of health rather than into that of disease.

Importantly, however, Boorse's solution relies heavily on the possibility of making a clear distinction between a disease and its causation. Yet, it could be asked whether such a distinction can be drawn so easily. Even if it may be possible to distinguish a disease from its external factors, it is not clear that it is always possible to distinguish between a disease and its internal, physiological risk factors, as in the case regarding the main risk factors of cardiovascular diseases such as progressive atherosclerosis and hypertension. There is something rather strange about reducing the long and incremental process of atherosclerosis to a 'disposition to become diseased under certain conditions'.

As stated above, the status of conditions such as hypertension and hypercholesterolemia appears to be very ambiguous. They do not seem to be reducible to 'risk factors' that can be clearly demarcated from the category of 'disease'; in medical usage, they are often seen as pathological states. Peter Schwartz introduced the notion of 'risk-based disease' for these kinds of conditions. Nevertheless, he maintains the possibility of a distinction between risk and disease (and thus, also between preventive and curative medicine) even for those conditions. For Schwartz, the superiority of functional accounts of health, like BST, is precisely that they make it possible to clarify the status of risk-based diseases. His analysis could be interpreted as stating that when 'risk-based diseases' like hypertension are not associated with pathological complications, i.e., dysfunction, these conditions should not be seen as pathological (and so should not be called 'disease' at all). In the case of blood pressure, for example, the WHO (World Health Organisation) recognises three levels of hypertension. If the blood pressure is elevated more than a certain amount above normal—what is called level 2 or medium-severe hypertension (i.e., systolic blood pressure 160–179 mmHg and/or diastolic blood pressure 100–109 mmHg) and level 3 or severe hypertension (i.e., systolic blood pressure 180 mmHg or higher and/or diastolic blood pressure 110 mmHg or higher)—there will be functional consequences or damage to vital organs such as the heart, brain, kidneys, and eyes. In both cases, there is dysfunction and thus pathology. This is not the case regarding level 1 hypertension or mild hypertension (i.e., systolic blood pressure 140–159 mmHg and/or diastolic blood pressure 90–99 mmHg). In that case, according to Schwartz, what justifies (a preventive and not a curative) treatment is not the presence of a dysfunction but simply that the risk of disease is higher without treatment. And, the dysfunctional account of disease does not see level 1 hypertension as a disease.

But Schwartz' analysis is on a wrong track and it fails to clarify the status (normal or pathological?) of 'risk-based disease'. I consider that the main point that first needs to be recalled about risk-based diseases such as hypertension or hypercholesterolemia is that they are physiological variables that are biological indicators (or physical magnitude) of functioning but not direct expressions of functioning.[8] It should be recalled that BST's notion of function refers to the

[8] Some clarification of the meaning of functional efficiency in the BST and of the confusion introduced by the frequent close correlation with some biological indicator of functioning has recently been given by Hausman [24] and by Boorse himself in an unpublished paper: 'Clinical Normality'.

efficiency of the process, i.e., its contribution to physiological goals.[9] The notion of function, understood as contribution to the goals of survival and reproduction of an organism, should thus be distinguished from the *concrete process* making the physiological contribution. Most basic standard laboratory or clinical tests are not, as Boorse points out, direct tests of function, but of some quantitative information correlated with function, or of the concrete process [4]. Schwartz has paid insufficient attention to BST's notion of efficiency contained in Boorse's concept of function.[10] He does not seem to see that even medium (or severe) hypertension in itself is probably not a dysfunction, or at least, not a direct expression of a subnormal functional efficiency, but rather a mere quantitative variable indicative of the level of functional efficiency of the circulatory system. If one adheres strictly to BST's way of determining the normal level of functioning, the population distribution should be that of the functional efficiency associated with blood pressure and not the simple level of blood pressure. A correct understanding of the notion of functional efficiency suffices to explain why parameters concerning the population distribution of a variable (the normal range), such as blood pressure, do not allow one to make a distinction between the normal and the pathological: the level of blood pressure is not in itself a direct measure of functional efficiency.[11] Even if blood pressure were regarded as a functional process, its normality should be defined with respect to its efficiency, which is certainly not reducible to its mere level.

Once one recalls this central but often neglected aspect of BST, the problem of the normal-pathological demarcation in the case of risk-based diseases like hypertension or hypercholesterolemia (second section) seems to disappear, or at least be mitigated. But it does not overcome the core objection against the relevance of relying on statistical normality to define health, just as it does not overcome the problem of practically establishing the demarcation between the normal and the pathological. Even if it were possible to obtain a population distribution of the functional efficiency associated with blood pressure, rather than the level of blood pressure per se, can one assume that the form of this distribution would be a continuous bell curve, such that the limit between the normal and the pathological could be conventionally chosen, as is the case in any application of statistical normality to a continuous distribution?

[9] To quote Boorse: 'the function of the thyroid is not merely to secrete hormones, but to secrete the right amount of them for current metabolic needs' [3].

[10] With this in mind, and as mentioned briefly above, Schwartz's proposal to solve the problem of common diseases by adding a third axis, an evaluation of 'negative consequences', to the two axes of BST's bell curve (statistical distribution and functional efficiency level) appears somewhat strange. Boorse's notion of function already includes some *consequences* or *effects* of a process or trait, namely, its efficiency or contribution to individual survival and reproduction. See also Hausman [24, p. 527].

[11] Likewise, the criticism of BST I made in the section 'The Risk Approach and the Normal-Pathological Distinction', where I pointed out the problem of using the statistical distribution in the case of the demarcation between normal and pathological blood pressure, did not yet take account of this aspect of BST. It should be recalled that, for Boorse, pathology consists in statistically subnormal *functional efficiency* and that the statistical distribution to which the definition refers is related to *functional efficiency*: the normal level of functioning is 'at *efficiency* levels within or above some chosen central region of their population distribution' whose two axes are statistical distribution and functional efficiency. This means that a disease is not reducible to a complete failure to function but could simply involve inadequate functioning.

Ultimately, there is no reason to suppose that the distribution of functional efficiency should be bell-shaped, unimodal, and continuous [24, 25]. As we will see in the following section, it seems more appropriate to abandon the idea that statistical normality serves to *define* the difference between the normal and the pathological, even if prevalence is very useful in practically approaching it. Moreover, this clarification of what the exact consequences of risk-based diseases are for BST ultimately highlights how problematic the definition of functional efficiency is; this problem is hardly confronted by Boorse, who proposes a concept which reveals to be very abstract and 'theoretical' (in the sense of being far removed from practice).[12] In practice, in laboratory or clinical tests, this demarcation between the normal and the pathological—based on the level of functional efficiency on one axis and the statistical distribution on the other—appears almost impossible to determine. Physicians thus use rough biological indicators rather than direct tests of functional efficiency. This highlights how important the gap is between the practical and the theoretical concept of health and disease in BST.

To sum up, a way to avoid the problem of risk-based disease, as raised by epidemiology, is to maintain a distinction between risk and disease and to limit the influence and role of epidemiology in our medical knowledge to disease aetiology and preventive medicine. The distinction between intrinsic health and instrumental health allows BST to take into account some disease risk variations or 'risk factors' without identifying them with diseases. But, as I have shown, this interpretation relies on a problematic distinction between internal and external disease factors, especially in the case of 'risk-based diseases', and Schwartz's attempt to clarify their status is not convincing. Moreover, it appears that the problem of defining and practically measuring functional efficiency is hardly confronted by BST. In the following section, I suggest that by granting epidemiology a theoretical role in constructing our knowledge of health and disease, some of the difficulties encountered above could probably be overcome.

Towards an articulation between physiological and epidemiological knowledge about health

In this last section, I will sketch how problems encountered by BST could be better explored, and perhaps even solved, by taking into account the epidemiological point of view on health and disease, seen as distinct but complementary to physiology. I thus suggest that epidemiology should be seen as contributing to our theoretical knowledge of health phenomena, alongside physiology. A more robust argument for that claim would, however, require further investigation and analysis.

Statistical normality as a guide not a part of the theoretical definition

In BST, statistical normality determines the level of adequate functioning, that is, the demarcation between normal and pathological levels of functional efficiency in

[12] See also Hausman [24]: 'Boorse says little about what defines efficiency and how its levels are to be distinguished, as they must be before one can talk about their frequency and draw a graph'.

a particular reference class. But is statistical normality simply an indicator or guide for those practical and clinical aspects of medicine that require a distinction between health and disease, or is it a part of the theoretical definition of normal functioning? Both descriptive epidemiology and analytic epidemiology depend heavily on statistics. Nevertheless, as shown in the two preceding sections, neither form of epidemiology supports a statistical concept of normality. This could be seen as reinforcing Hausman's defence [24] of the first option of the above-mentioned alternative (i.e., that statistical normality is simply a guide for practical decision in medicine); to Hausman, efficiency is not determined by prevalence. I thus follow Hausman in denying the identification of adequate functioning with statistically normal functioning; that is, I abandon the idea that prevalence serves to *define* health. As Hausman puts it, 'the functional efficiency theory, in contrast to BST, denies that prevalence defines whether a level of functional efficiency is healthy or pathological' [24, p. 536].[13]

What is crucial in Hausman's theory of health is the determination of 'the magnitude of differences in functional efficiency' rather than 'the location of a level of functioning in the distribution of levels' [23, p. 536]. He is concerned with the *differences in efficiency* rather than where the difference between the normal and the pathological lies in the overall distribution. Thus, for Hausman, there can be theoretical distinctions between 'more or less healthy' states without a theoretical breakpoint between disease and health. Hausman's 'functional efficiency theory' thus implies renouncing the theoretical status of the distinction between health and disease even as it maintains that statistical normality could be a useful guide for the *practical* concept of normality: 'statistical normality remains a useful—indeed a crucial—guide to the practical distinction between health and pathology, but it does not define the difference, and, in any case, for theoretical purposes, the distinction does not need to be drawn at all' [24, p. 540]. Health can be naturalistic without requiring statistical normality: it is simply the contribution to fitness and to goals of systems within organisms. What is 'naturalistic' in his theoretical concept of health is the standards employed in the assessment of functional efficiency, i.e., what defines greater health and allows one to compare different levels of health.

The epidemiological risk approach is inherently comparative. As I alluded to before, analytical epidemiology studies inter-individual and inter-group variability, making comparisons and drawing inferences on risk from these comparisons. This supports Hausman's interpretation and analysis of the naturalistic view of health in medical sciences as focusing on the magnitude of differences in functional efficiency rather than the determination of a normal level of functioning. Granting epidemiology a theoretical role in defining health, it could be said that epidemiology reinforces the importance of a comparative view of health over a non-comparative one. Yet, where my approach differs from Hausman's naturalistic account is precisely in the fact that it attributes this role to epidemiology, alongside physiology. Hausman's analysis of functional efficiency theory, by contrast, remains in line with BST's central and univocal focus on physiology. Thus, unlike

[13] Hausman states, 'statistically normal function often coincides with adequate functioning, but one should not identify the two' [24, p. 525].

Hausman's theory, the health concept that follows from my approach is more than a 'modification' or a 'reinterpretation' of Boorse's theory [24, p. 550].

A more empirical approach to the reference classes

In BST, the notion of physiological function is relative to a reference class characterised as an 'empirical ideal' by Boorse. It is true that the relativity of functional assessments to a population is a necessary condition for generalisation in health judgments. However, I have shown, in the second section above, the difficulties encountered by BST in defining what the appropriate reference class is in an empirical and objective way. On the one hand, BST's reference classes prove to be more *ideal* than *empirical*, and their definitions are more arbitrary than Boorse claims. On the other hand, medical judgments prove to be more sensitive to the evolution of health patterns in human populations than the stability of a natural functional design assumed by Boorse's view of physiology.

If epidemiology is considered to contribute to the medical concept of health, the manner in which it relies on population relativity in its approach to health phenomena could be instructive: the population is context-dependent and particular. There is no one unique way, but only different possibilities, for defining different groups and subgroups in which health phenomena will be described and their determinants analysed. This relativity is compatible with a scientific approach, as shown by the fact that in epidemiology, the reference population used in the study is explicitly mentioned and even carefully defined and delimited. Moreover, empirical and statistical techniques for assuring both objectivity and adequate means to evaluate the representativeness of a population are used to determine the status and characteristics of the study sample and the limits of validity or of certainty of any inference. Further work needs to be carried out to characterize the epidemiological concept of population, but it could already be said that epidemiology encourages one to consider the population of reference required by health judgments to be less absolute and more context-dependent than in BST. The population to which scientific health judgments are relative is probably a mix between, on the one hand, a certain ideal, abstract, and stable reference class assumed by physiology, and, on the other hand, the empirical, concrete, and study-dependent populations of epidemiology. Here again, my approach differs from Hausman's 'functional efficiency theory', which maintains the notion of a natural species design [24, pp. 538–540]. Once again, then, it would seem that giving a theoretical role to epidemiology challenges more than supplements BST.

It could be added here that epidemiology is also one of the main ways to introduce and study the role of the environment in health. It would certainly help in delimiting normal and abnormal environments, or at least, healthy and unhealthy environments. In what manner this aspect should be integrated into the definition of health remains, however, an open question.[14]

[14] For an attempt in this direction, see Venkatapuram [26].

Risk approach as a determination of functional efficiency

In highlighting misconceptions about functional efficiency above (in the section on 'risk-based diseases'), I stressed the fact that the question of how to define functional efficiency is hardly taken up by Boorse. A clear role could be given here to epidemiology. If functional efficiency is the contribution to fitness and to the goals of systems within organisms, the epidemiological risk approach appears to give a direct estimation of the level of functional efficiency of a part or a trait. The correlation of the level of a variable with its consequence in terms of probability of survival, which is at the core of cohort and case–control studies, could be seen as providing a measure of the physiological contribution of a trait (or process) to individual survival. At the very least, this correlation delivers a better estimate of the functional efficiency of a trait than the population distribution of variables such as blood pressure or blood cholesterol levels. In addition, it also explains why contemporary medicine uses epidemiological findings on these physiological variables rather than their statistical distribution to determine the demarcation between the normal and the pathological.

In such an interpretation of the role of the epidemiological risk approach, the correlation gives a *partial* determination—partial since the contribution to reproduction is not here taken into account—of BST's functional efficiency. But in considering that epidemiology contributes to knowledge about health and disease, we may find that reproduction in medicine is not as relevant as survival. The endpoint in etiological studies is often disease incidence rate or mortality. Survival (or life without disease) prevails over reproduction. This aspect corresponds to the recent criticisms of the equal weight given in BST's definition of a physiological function to survival *and* reproduction. Reproduction in particular is a problem for fitting medical usage, since it seems to imply the inclusion of homosexuality in the pathological. Jerome Wakefield thus added a 'harmful' component to dysfunction in his definition of disease [27]. Another criticism is that, for the elderly, functional contribution to reproduction does not make any sense. According to Schwartz, one should say survival *or* reproduction rather than survival *and* reproduction, but such a modification may raise problems for Boorse's account of function [16]. Hausman similarly considers that we may at some points substitute inclusive fitness, and at least consider that 'the parts of organisms have specific goals, which generally, but not always, contribute to survival or reproduction' [24].

Thus, rather than thinking that the epidemiological risk approach only delivers a partial approximation of theoretical health, it could be interpreted as indicating that survival is more important in theoretical and medical judgments on health than reproduction. It can even be said that the risk approach probably contributes to determining functional efficiency.

Concluding remarks

My exploration of the relations between BST and epidemiological findings on health phenomena has led to clarifications of the true limits of BST's concepts of 'statistical normality' and 'reference class', as well as to a novel presentation of

some of BST's difficulties already pointed out by its critics. The 'epidemiological transition' led me to consider the importance of the chronicity of diseases in the well-known problem of typical or common disease and, thus, to show that the amendments or reinterpretation of BST aimed at solving this problem ultimately bring to light the difficult issue of how to define objectively the time-slice extension of the reference class. Moreover, the risk approach of analytical epidemiology also highlights the limits of a categorical way of thinking about health and disease as mutually exclusive states. The exploration of a possible distinction between the categories of 'risk factor' and of 'disease' (preventive and curative medicine) led me to stress how enigmatic the definition and distinction of levels of functional efficiency is in BST.

In addition, the epidemiological point of view has made it possible to consider various ways in which this discipline contributes to a better understanding of our contemporary medical concept of health. In particular, I suggested taking the further step of accounting for the epidemiological as much as the physiological approach when defining the theoretical concept of health. Epidemiology makes various useful contributions regarding the question of how to define functional efficiency as well as to the question of what constitute reference classes. In addition, it encourages abandoning the theoretical role of statistical normality in defining the demarcation of the normal and the pathological, as well as BST's belief in an absolute distinction between health and disease, which should thus be replaced with a comparative concept of health. These elements may allow for a better description of the medical concept of health in contemporary medicine. If aspects of my approach are similar to parts of Hausman's reinterpretation of BST, I hope to have shown that, contrary to Hausman, I arrive at those elements through the epidemiological point of view. In this, and in granting epidemiology a theoretical role in the definition of health and disease, my account could thus be said to constitute a new way of arriving at a naturalist concept of health. The account of health that emerges from this approach is naturalist in the sense that it takes into account the way biomedical sciences theorize and explain health and disease and not only an analysis or description of scientific usage and health judgments.[15] But further analysis needs to be carried out regarding the specific role of epidemiology in theoretical analysis as well as in the explanation of health and disease phenomena, if we are to arrive at a precise formulation of epidemiology's contribution to defining health and disease.

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[15] I rely here on the distinction introduced and stressed by Boorse himself between his naturalism and that of Murphy: 'To Murphy, the best characterization of mental disorder as a theoretical concept must emerge from scientific theorizing, not analysis of scientific usage' [28, p. 20]. Analysis of scientific usage is naturalism of one kind—that advocated by Boorse—whereas when physiology joins in scientific theorizing, it is naturalism of a different kind—that advocated in Murphy [29] or Lemoine [30]. My account resembles Murphy's or Lemoine's type of naturalism.

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