

Holism and Reductionism in the Illness/Disease Debate

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(Penultimate version. To be published in S. Wuppuluri and I. Stewart (eds.), *From Electrons to Elephants and Elections*, https://doi.org/10.1007/978-3-030-92192-7_39)

Abstract

In the last decades it has become clear that medicine must find some way to combine its scientific and humanistic sides. In other words, an adequate notion of medicine requires an integrative position that mediates between the analytic-reductionist and the normative-holistic tendencies we find therein. This is especially important as these different styles of reasoning separate “illness” (something perceived and managed by the whole individual in concert with their environment) and “disease” (a “mechanical failure” of a biological element within the body). While the demand for an integrative view has typically been motivated by ethical concerns, we claim that it is also motivated, perhaps even more fundamentally, by epistemological and methodological reasons. Evidence-based bio-medicine employs experimental and statistical techniques which eliminate important differences in the ways that conscious humans evaluate, live with, and react to disease and illness. However, it is precisely these experiences that underpin the concepts and norms of bio-medicine. Humanistic disciplines, on the other hand, have the resources to investigate these experiences in an intersubjectively testable way. Medicine, therefore, cannot afford to ignore its nature as a human science; it must be concerned not only with disease and illness, but also with the ways in which patients as persons respond to malady. Insofar as attitudes and expectations influence the criteria of illness and disease, they must be studied as part of the genuine subject matter of medicine as a human science. In general, we urge that this is a necessary step to overcome today's trend to split evidence-based and clinical medicine.

1. Introduction. The Two Souls of Medicine and the Illness-Disease Dichotomy

1.1 Medicine: Two Souls for a Single Science

Dissatisfaction with biomedicine, and more generally with a medicine modelled after and depending upon biomedical sciences and technology, is spreading more and more; not only among patients (who often are turning to

“alternative”, “holistic” or “complementary” forms of medicine), but also among health care professionals and, particularly, medical doctors (cf. Cole & Carlin, 2009). On the one hand, medical doctors retain the ambition to be scientists—an ambition which is also reflected in the English language (they are also designated by the term “physician”, whose Greek-Latin origin, “physicus”, means “the one who knows nature”, i.e., the scientist in its widest sense). On the other hand, many physicians and healthcare professionals are aware of the need of personalizing the traditional and biomedical model of medicine (cf. Engel, 1978: 169; Glick, 1981 p. 1037; Willis, 1989; Marcum, 2008), a need that is reflected by the term “clinician”, faithful to its Greek origin, *clino*, probably meaning bending towards, or lying on, the sufferer’s bed.

It is therefore no accident that in the literature of the last decades about the status of medicine, there is a new awareness that an adequate notion of medical praxis requires an integrative position, which mediates between the analytic-reductionist and the normative-holistic perspective (cf. Wyss, 1986; Nordenfelt, 1986, 1997a, 1997b, 2013; Christian, 1989; Hahn, 2000: 35–53; Pieringer & Fazekas, 2000: 89– 111; Marcum, 2008; Larkin et al., 2011: 318–337). This is not a recent demand. Karl Jaspers already fully understood, as early as 1919, the importance of reconciling the two “souls” of medicine (Jaspers, 1919: 59), i.e., the analytical-reductionist and the holistic-normative, or, the scientific-technological (practised by the physician) and the clinical (practised by the clinician). Jaspers’s problem fully corresponds to today’s physician-clinician antinomy. The associated need to reconcile the scientific soul and the clinical soul of medicine (on which see also Jaspers, 1958: 1038, Engl. Transl., 255) is as (or more) urgent today as it was in Jaspers’s time.

1.2 The Illness-Disease Dichotomy: A Part-Whole Puzzle

Now, since the duplicity of attitudes towards the patient corresponds roughly to what we usually designate as “disease” and “illness”, it is possible to take an important step towards achieving the just-mentioned goal if the relationship between these two meanings of malady is correctly set up (the word “malady” will be used here in the most generic sense, which includes not only “disease” and “illness”, but also “sickness”, and the sense of being unfit or unable to do what you want to, when you want to). As Cassell noted in 1976, the technological revolution, by fueling the hope of curing many maladies, has contributed to an increasing differentiation between what could be treated by technological means (with an often excessive confidence and hope) and illness, something which is subjective, it is something the person “lives through” as a whole, and therefore does not fit into the categories of rigorous technoscience. Typically, prospects for successful treatment were significantly less, when not wholly abandoned:

The success of medicine has created a strain: the doctor sees his role as the

curer of disease and "forgets" his role as a healer of the sick, and patients wander disabled but without a culturally acceptable mantle of disease with which to clothe the nakedness of their pain. (Cassell, 1976: 27)

Notwithstanding the ongoing debate about disease and illness, there is some agreement that "disease" and "illness" are the key concepts of the opposite trends, the analytical-reductionist and the holistic-normative, in conceiving both malady and medicine. From this point of view, the mentioned demand for an integrative position concerning the status of medicine, which combines the analytic-reductionist with the normative-holistic perspective, must also be raised for the distinction between disease and illness.

1.3 Can a Human Science Be a Science? Human Sciences and Objectivity

As just noted, clarifying the relation between the two faces of malady expressed by the terms "disease" and "illness" is crucial for creating an integrative view capable of overcoming the opposition between the reductionistic-analytical and the holistic-normative perspective of medicine. However, the demands for such an integrative view must not only be connected with ethical reasons or reasons of practical desirability (which will not be taken into consideration here), but first of all with epistemological and methodological reasons, intrinsically linked to the status of medicine as a science: human, yet science. Medicine, in every aspect of its activity (including its disciplinary and institutional organisation), must reconcile the scientific-objective and impersonal dimension (mainly expressed by the term "disease") with its clinical and personal dimension (mainly expressed by the term "illness"). This, as we shall try to show, is required by the nature of medicine as a human science, a nature that must also be taken into account in order to increase its own degree of scientificity, objectivity, or intersubjective controllability. Obviously, medicine is not to be considered a human science in the restrictive sense that it must be "humanitarian" (a welcome property, of course), but as having a methodologically specific object of investigation, that is, beings which are biological organisms, and, at the same time, operate as more than mere biological organisms, that is—to remain as neutral as possible with respect to a difficult philosophical debate—as cultural-biological entities.

We propose to show that there is an aspect of "illness" that is central in both dimensions of medicine. This aspect is at once objective and intersubjectively controllable, yet also characteristic of the human sciences and not completely reducible to the natural sciences. Specifically, illness depends not only on the physical and biochemical reality of the patient's body, but it includes the cultural side, which is always involved in the particular way in which patients live, and respond to their own experience of illness. The way in which patients live their illness, both on a personal and social level, is not only influenced by

natural constraints (such as the fact of possessing a certain body structure or, to put it as Boorse does, a certain “species design”), but also by law-like cultural constraints. Even the domain of the experience of illness, like those dealt with by the other human sciences, is subjected to regularities that add to, and interfere with, those that physical and biochemical investigations highlight. It is only by taking them into account, therefore, that it is possible to increase the ability of medicine to prevent, diagnose and treat illnesses in an increasingly effective way. In other words, the interpersonal and social side of illness can and must be investigated from the point of view of medicine as a science. Both the bio-physician and the clinician cannot ignore, each from their own point of view, the patient’s attitude towards their illness and the development of the patient’s ways of coping with the illness, which are not only of paramount importance for any therapy, but also for any diagnosis. An approach to medicine that would try to leverage exclusively the biological aspect of the disease (as was for example the explicit intent of Boorse’s famous essay of 1977, in accordance with a naturalistic-statistical view of biological normality inaugurated by Claude Bernard in 1865), would not only be a medicine that would break that physician–patient alliance, which obviously no medicine can disregard, but it would be a medicine unaware of its nature as a human science.

1.4 The Treatment Plan

The present paper is organized as follows. Section 2 describes two important but opposite conceptions: health and malady (understood as a lack of, or contrary to, health: see, e.g., Sadegh-Zadeh, 2012: 153–154). It explores certain difficulties with each, which together lead to a kind of antinomy, which, as shown in Sect. 3, also affects the few attempts to offer an integrative view of health and malady (the most important of which is perhaps that of Wakefield: see e.g., 1992, 2007, 2014, and 2015). Section 4 shows that the strengths of both the naturalistic, analytic-reductionist and the normative, holistic-humanistic conceptions can be preserved, on different levels, if one understands in what sense medicine is a human science. Section 5 considers the case of statistics (seen as a process of generalising from individual observations) when applied to human sciences. Section 6 builds a proposal for epistemic reconciliation and integration of naturalistic and normative standpoints.

2. Health, Disease, Illness: Analytic-Naturalistic Versus Holistic-Normative Perspectives

2.1 Two Accounts of Health and Malady

Two main accounts of health and malady are distinguishable in the literature, even if this distinction runs the risk of a certain oversimplification (cf. Simon, 2007 and Kingma, 2014). The two key concepts that correspond to

these two different conceptions of health and malady are “illness” and “disease.”

On the one hand, the first view—sometimes defined as naturalism, or an analytic-naturalistic perspective—puts particular emphasis on the term “disease”, something which can and ought to be objectively, scientifically ascertained and localized within the patient’s body. This is very clear in the thought of Christian Boorse, the best-known and most discussed exponent of such a naturalistic view. According to Boorse, we have to distinguish between “illness”, which is a concept dependent on a cultural context, and “disease” (or “pathology”, as he prefers since 2014: see Boorse, 2014), a descriptive, non-normative concept, whose main elements are biological function and statistical normality. “Disease” could be defined as

a type of internal state which is either an impairment of normal functional ability, i.e., a reduction of one or more functional abilities below typical efficiency, or a limitation on functional ability caused by environmental agents. (Boorse, 1977: 567; cf. Boorse, 2014: 683–684)

Typical or normal performance is defined by the concept of “species design”:

Our species and others are in fact highly uniform in structure and function; otherwise there would be no point to the extreme detail in textbooks of human physiology. This uniformity of functional organization I call the species design. (Boorse 1997: 557; see also Boorse, 2014: 39)

From this point of view, Boorse opts to understand the concept of health as the absence of disease:

Health as freedom from disease is then statistical normality of function, i.e., the ability to perform all typical physiological functions with at least typical efficiency. This conception of health is as value-free as statements of biological function.¹

More generally, it might be said that, as far as “disease” is concerned, it is possible to distinguish two main components: from the point of view of its contents, essential ingredients of “disease” are biochemical, genetic, and functional-physiological (in short: biological) elements, so that ‘disease’ may be observed, examined, and measured in an intersubjectively testable way; however, from the point of view of its social-cultural-linguistic classification, what a ‘disease’ is, is determined by the theoretical lenses and the particular practices of health professionals: in this sense, because they are the undesirable

¹ Boorse (1977): 542. Though interpreted variously, Boorse’s conception has been taken up by several authors: see, e.g., Taljedahl (1997), Williams (2007) (who treats disease in terms of distortions of standard cellular network processes), and Ananth (2008).

conditions that health professionals de facto happen to treat, diseases vary over time with evolving historical and social conditions (see e.g., Boorse, 1977, Kleinman, 1988: 4; Aho & Aho, 2008; Sadegh-Zadeh, 2012: 151– 153; on this point see also Grmek’s important notion of “pathocoenosis” (Grmek, 1983, Engl. Transl., 2-3).

On the other hand, according to a second view—which finds its pivot in the term “illness” and is sometimes defined using a normativist or holistic-humanistic perspective—both health and malady must be defined by an explicit or implicit choice or convention concerning the goals we have for our own lives. In this connection it is generally held that the term “illness” encompasses feelings, beliefs, and attitudes regarding bodily and mental conditions that overtake and impede us in performing the tasks and in the interpersonal interactions of our life (e.g., we may be unable to walk or drive because of back pain) (see e.g., Kleinman, 1988: 3; Aho & Aho, 2008: 3; Hofmann, 2017: 16). This is the reason why disability (more precisely, any limitation in whole-person activities, as per the World Health Organisation definition: World Health Organisation, 2001) has to be considered here as a form of illness.

Here too we may distinguish two main components. On the one side (from the point of view of its contents) important ingredients of “illness” are psychological states such as pain, suffering, anxiety, fear, and behavioural disturbances like disability: all phenomena being undesired and medically treated, not less than bone fractures and myocardial infarctions. In this respect, the relationship between illness and health surfaces clearly. On the other hand (from the point of view of its social-cultural-linguistic classification), what an illness is, is determined by a lived experience, both at the personal and social levels.²

An important point in this context is that illness is usually connected to the wholeness of the individual person’s feelings (which in turn largely reflect the interpersonal and social relationships in which the person is involved). This point was finally transposed by the World Health Organization (WHO) into its famous definition of health (“a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”), whose defects do not exclude that it had the merit of connecting the ‘normal functioning’ of the body to the more general well-being of human life, considered both in its psychological and social dimension.³

² In this last case, in accordance with the work of Parsons about the “sick role” (Parsons 1951, 1975), “sickness” is the more often used term, but it will be included here under the umbrella of “illness”, which emphasizes the interpersonal and social aspect (consistent with this, in common parlance, is calling work absences due to health care problems “sick” leave). On this point see also Twaddle (1968, 1994a, 1994b), who was one of the first authors to distinguish between disease, illness, and sickness.

³ Callahan (1973: 86). For the second view, see e.g., Veatch (1973: 524–5), Engelhardt (1975, 1984, and 1996), Margolis (1976); Schaefer (1976: 20–21); Engel (1978); Whitbeck

The distinction we have been drawing has been concisely expressed by Cassell in writing that “[d]isease [...] is something an organ has; illness is something a man has.”⁴ With a more explicit reference to the subject of our paper, Nordenfelt spoke of two perspectives from which ‘health’, ‘disease’, and other similar concepts may be interpreted: the “analytic” (or “atomistic-biological”)—sometimes defined as naturalism—and the “holistic” (or “holistic-humanistic”) perspective. From the former perspective, a person is mainly regarded “as a complicated biological organism with a vast number of interacting parts”, and the central concepts are biological, chemical, and statistical; from the latter, “man is taken to be fundamentally a social agent, a complete human being acting in society. On such a platform the theory construction will primarily use humanistic or social concepts. The concept of a person is central, so are the concepts of action and goal.” (Nordenfelt, 1986: 281) From the former perspective, again, “one directs one’s attention to particular parts of the human organism, and considers their structure and function”; from the latter, “one focuses on the state of the human being as a whole, and judges whether he or she is healthy.” (Nordenfelt, 1995: xiii) In this latter sense, health

has its locus on the level of the whole person. A human being as a whole can be healthy. It is not molecules or tissues which are healthy. We may say metaphorically that a heart or a lung is healthy, but what we then mean is that this heart or lung contributes to the health of the whole person. (Nordenfelt, 1997a: 244)

2.2 *Irreconcilable Perspectives?*

(1981a; 1981b; 1981c), Nordenfelt (1984, 1986, 1995, 1997a, 1997b), Reznek (1987), Pörn (1993), Wieland (1995, 2002), Fulford (2001). As far as the notion of “illness” is concerned, phenomenological literature is also very important, starting from Merleau-Ponty (1945) up to the most recent works, among which see at least Zaner (1981), Toombs (1992), Aho and Aho (2008), and Svenaeus (2000, 2014). But already in antiquity Seneca had given voice to “illness” by trying to define maladies in subjective terms: “Triae haec in omni morbo gravia sunt, metus mortis, dolor corporis, intermissio voluptatum.” (Epistulae morales ad Lucilium, 78, 6.).

⁴ See Cassell (1976: 27). The relation between a focal localization of malady and its pervasive affection of the self, reflects itself in the English language, which distinguishes between “pain” and “ache”: one speaks of knee pain and skin pain, but of headache, toothache and stomachache, and depending on his/her experience, the patient may speak of back pain or backache. Neo-Latin languages have difficulties in recognizing this distinction: for instance, there were problems translating into Italian a famous English questionnaire asking whether your pain is of “aching” quality. The proposed solution was translating “aching” as “dà sofferenza” (“it makes you suffer”) (Maiani and Sanavio 1985). However, both in English and in Italian, “suffering” defines a domain much wider than “suffering because of pain” does. In building a back pain questionnaire including the “aching pain” item, the Authors found that only some of the Italian participants perceived “dà sofferenza” as a specific qualifier, rather than a synonym, for pain (Tesio et al., 1997).

Despite attempts to heal the disease/illness dichotomy, it remains deeply rooted in contemporary medicine. Take the cases of disability and mental health. The World Health Organisation periodically updates the International Classification of Diseases (ICD), used worldwide in epidemiology and clinical practice (for the latest, 11th version see: <https://www.who.int/classifications/classification-of-diseases>; accessed Dec 28th 2021). Biological “diseases” are loosely related to functional consequences at the whole-person level, i.e., the level of behaviours and psychological states. Therefore, in 1980, the WHO strove to separate the “functioning” of body parts (related to “impairments”) from the functioning of the person as a whole with respect to the outer world (related to “disabilities” and “handicaps”). In this sense, a brain junction gap caused by an infarction would be an impairment, while the reduced capacity to walk or to communicate (i.e., needs shared by all human beings) would represent disabilities, and finally, if an individual person needed to abandon a job, or be absent from school, this would be a handicap. In 2001, for the WHO, “disabilities” became “activity limitations”, and “handicaps” became “participation restrictions”, but the distinction with respect to impairments (a whole-parts distinction) remained sharp. And again, both the WHO and the American Psychiatric Association (2013) do not speak of mental “diseases” but of mental “disorders” instead.

It is therefore no accident that the ensuing discussion has brought to the fore a kind of antinomy, which arises from considering one side of health or malady in abstraction from the other. Against the internal coherence of a merely descriptive-naturalistic account of disease, it has been argued that having a particular digestive or breathing system, and/or particular reproductive organs, represents already a potential set of behavioural patterns or norms to be followed by an organism, and these norms are indirectly brought to light whenever the ‘normal’ functional ability of an organ is reduced or limited to some extent.⁵

⁵ Cf. above all Canguilhem (1972) (which, in a certain sense, can be regarded as a worthy *ante litteram* critique of Boorse), Toulmin (1976), and Fedoryka (1997). Important pages have, however, been written on several occasions by Engel on this point (see for example 1978 and 1979). Engel put into question a biomedical model which requires both that disease be dealt with as an entity independent of social behaviour (which implicitly assumes mind–body dualism), and that behavioural deviations from the population’s mean are to be explained only on the basis of biochemical or neuro-physiological processes (which implicitly assumes reductionism). O’Leary’s thesis that Engel’s “bizarre insistence that dualism and reductionism are one and the same view” (O’Leary 2020), is a misunderstanding of Engel’s basic idea, which is very simple: if one accepts a dualistic paradigm such as the Cartesian one, one also accepts the idea that only the body (mechanistically conceived), as opposed to the soul (which is immaterial), can fall ill, but then, the tendency naturally follows according to which the doctor must only deal with the body and neglect the mind: which is precisely, in medicine, the reductionism combined with the dualism of which Engel spoke.

In other words, simply claiming that some body functions are fundamental already assumes that they were embedded in a teleological system of aims or values, and the assertion that an organ functions well already presupposes that this is something which we *should* preserve in its present state. No appeal to a particular species design can avoid a rationally unjustifiable jump from ‘is’ to ‘ought’.

2.3 *Splitting the Normal and the Pathological*

As we have just mentioned, the inherently normative nature of any kind of “normality” has already been asserted by some authors. However, to be fair, Boorse is much more aware of the difficulties facing his account than his critics have usually assumed. His proposal is that neither the mere recourse to the species design (ultimately appealing to a Darwinian fitness-selection model, see Garson, 2016) nor to statistical normality provides a satisfactory definition of health or disease. Both are necessary to do this.

But here it can be said that two mistakes fail to make a truth. It is not so much a question of solving the problems raised by some counterexamples, some of which Boorse admits that he has to solve with an ad hoc exclusion (specifically, the case of “universal diseases”, such as dental caries and some geriatric or epidemic diseases, which are usually seen as pathological in spite of their being statistically very frequent phenomena: cf. Boorse, 1977: 566–567). Instead, it is a question of recognising that, in order to establish what health and disease are, the construction of a statistic is never value-free.

You cannot statistically determine what the nature of ‘health’ is in itself, since the production of statistics necessarily presupposes certain choices concerning the variables to be normalized and the “weight” to be assigned to these variables: these procedures, in turn, depend on evaluative elements (to say nothing of the choice of more sophisticated statistical models relying on complex assumptions). Any modelling is in itself a theoretic-normative process: for example, see the statistical ‘war’ between frequentists and Bayesians (cf. Mayo, 2018), and the recent surge against researchers’ faith in arbitrary levels of “statistical significance”, which are still the benchmark for decisions in most biomedical research (Amrhein et al., 2019).

2.3.1 Statistics Is Value-Laden

The natural environment is constantly changing (though, usually, very slowly compared to the duration of a human life), so that statistical ‘norms’, in a certain sense, must adapt: consider, as an example, how climate change and food availability impact the biological features and “diseases” of all living beings. However, the normative nature of statistics has in medicine further and distinct reasons, acting along the time-frame of human (and even individual) history (on this point see above all Canguilhem, 1972 and Wieland, 1995). First, humans

modify—in accordance with their interests and values—not only the natural environment, but also one another. It follows that the range of ‘normal’ values changes depending on new discoveries, social attitudes and political contexts, and the recognition itself of a given phenomenon as ‘normal’ (or, as a ‘disease’) is historically variable. In a society where body weight was assigned a great biological value there would be more tolerance of higher values than of lower ones. You would accept as ‘normal’ a positive statistical deviation from the average body weight much more in a society where thinness is an aesthetic ideal. To take another example, only in the late 1970’s did people begin to seriously consider “essential” hypertension as a “disease” in itself (the cause is still unknown, for which reason it is defined “essential”), but ‘normal’ values were very lenient, and very high pressure levels were accepted in elderly people. Nowadays, “essential” hypertension is considered as one of the most important causes of mortality and disability (Saklayen & Deshpande, 2016), and has generated huge statistical studies, which have set a much more restrictive range of ‘normality’. But perhaps the best example to show that the recognition of a given phenomenon as ‘normal’ (or, as a ‘disease’) is historically variable, is the “disease” drapetomania—which was supposed to induce slaves to run away and abscond (Cartwright, 1851/2004). Nowadays, no Ethical Committee would authorize studies on drapetomania (although forms of slavery, unfortunately, still exist; see <https://news.un.org/en/tags/modern-slavery>, accessed Dec 28 2021). In the same vein, homosexuality has long been classified as a psychiatric disorder. Nowadays, no Ethical Committee would authorize studies on the effectiveness of drugs claimed to correct “sexual orientations”. The latter are no longer classified as “diseases” or “mental disorders”, for either the World Health Organisation or the American Psychiatric Association.

In other words, not only does each statistical parameter depend on interests and values, both of which vary from individual to individual and from society to society, but—more crucially—interests and values can never be captured entirely by statistics, because these interests and values are key driving forces in changing the social environment as an essential ingredient of the criterion of normality. “Normality” is a value judgment as far as it describes ranges of societal tolerance not less than frequency ranges. An important lesson to be drawn from the examples provided above is not only that statistics cannot produce data that are completely neutral because they are based on the “nature” of things, but also that every statistic and every medical classification presupposes moral choices that, if they are to be made responsibly, require a rational debate not only on what the natural data or regularities are, but also on the values that we want to place at the basis of social (co)existence.

2.3.2 Statistics and Individuals Depend on One Another

However, there is at least one more reason—and perhaps this is even more

important in our epistemological and methodological context—that in one way unites, but in another distinguishes (again as normative) the use of statistics in the human sciences. There are no statistics concerning human behaviour (including those concerning illness or disease) that are not built from and controlled by resorting to, individual cases, that is, to the *interpretation* of individual behaviours or actions. To know whether a statistically significant number of patients have reacted positively to a therapy, one has to interpret not only signs, but also the patient's own answers to the clinician's questions. And this is not only the case when checking the effectiveness of a particular psychotherapy, but also the effectiveness of a vaccine or of a surgical operation.⁶

2.3.3 Is Paralysis of Lower Limbs a Pathology?

A simple thought experiment may serve to illustrate both points. Let us assume a highly developed technological society where people move, for short as well as long distances, by transport beams that send an individual's molecules from one place to another and reassemble the molecules upon arrival (for this example, cf. Buzzoni, 2003). As for the first point—that is, that statistical “normality” is value-laden, it can be easily deduced from what has been said: in such a society, an individual with both lower limbs paralyzed—or somebody suffering from any “pathology” involving a walking impairment—may be considered healthy or “normal” to the extent that he or she achieves the main objectives assigned to its individual members by that society; stated otherwise, he/she is healthy from the standpoint of “activity limitations”. More specifically, the person might not be disabled, according to the WHO glossary (Prodinger et al., 2016). As regards the second point—that statistics depend on considerations of individuals about themselves and other people—suppose you need to measure that person's level of independence in daily life (Tesio et al., 2002, 168–176) or satisfaction with life (Franchignoni et al., 1999). Cumulative questionnaires are needed (either self-administered or not) like in any measurement of behaviours, attitudes or perceptions (Tesio, 2003). These measures run the risk of being biased by the author's perspective (e.g., which items are selected for the questionnaire, and who determines their scores?) yet, they cannot be replaced by, say, biomechanical or neurophysiological measurements at the lower limbs (see Sect. 5 below for development of this idea). In using this perspective to ascertain whether a given person with paralysed or otherwise injured lower limbs has to be regarded as really healthy, one would already have overstepped the bounds of a merely naturalistic dimension of health and illness, for one would need to interpret reflections given by human beings about themselves and other people.

⁶ The relevance of patients' perspective is indeed more and more acknowledged in biomedical research: see the development of “patient reported outcome measures-PROMS” (Crossnohere et al., 2020).

2.4 Illness and Disease Are Not Fully Independent

One advantage of a biological definition of disease is that it can explain why a patient can be confident in estimations of their health, despite the fact that pathological changes are taking place in the body. A tumour can remain asymptomatic or regress spontaneously without necessarily having any effect on the subjective well-being of a person. The function of the immune organs is another illustration of the fact that the concept of health ought to refer to more than the level of subjective well-being. As Taljedahl (1997) noted against Nordenfelt (1993), when immune organs exert their capacity to combat infection,

they may give rise to symptoms that are transiently incapacitating, i.e., the expressions of bad health. Yet, these symptoms of bad health are in a sense also the expressions of good health. (Taljedahl, 1997: 68)

However, it can be easily shown that the relative ‘objectivity’, or even independence, of certain natural processes that occur in us, cannot justify any purely biological concept of disease. One can only conceive of the possibility of objective pathologies existing in the nature of things by indirectly connecting them with a subjective illness, which—in accordance with our past experience—indicates an objectively detectable disease. In a word, a disease is defined as a disease because it is acknowledged that sooner or later, in at least some of the affected people, it will lead to an illness. A skin nevus is not called a disease: although it is when it is recognised that it can become a skin tumour. A laboratory finding enables a physician to diagnose a disease not yet noticed by the patient, because the physician—in contrast to the patient—knows how to rank that finding in the context of a typical medical history. The physician can come to an assessment without having to rely on symptoms which occur later and are then felt subjectively, only because they know that, in the past, other individuals with similar, at first equally inconspicuous findings developed (inter)subjectively detectable symptoms after a certain period of time: this remains the necessary methodological starting point for an objective concept of disease. Without a direct or an indirect reference to these symptoms, that is, by entirely excluding the subjective feelings of illness, no laboratory result would ever be a meaningful (bio)marker of anything that might be called a “disease”.⁷ Before one can methodologically reconstruct a disease as the biological counterpart of illness, illness must be felt as such by some person, who, moreover, may have reached the awareness of being ill only through other people. If these “others”

⁷ On this, see Kumbhare and Tesio (2020); see also Buzzoni (2003). In particular, as far as “biomarkers” are concerned, see Buchner et al. (1999), and Taylor and Elston (2009).

are scientists, the person's illness can be framed in a taxonomic system of diseases (let us encase here also syndromes, i.e., sets of signs and symptoms, into the disease concept).

In a pathoanatomical dissection one does not see a disease or a diseased organ. One can just see an anatomical peculiarity, a difference from reference norms, to which one can attach the sense of a disease exclusively because, consciously or unconsciously, one relates them to ideas of unwanted suffering and death, which epistemologically precede the corresponding biological, metrical and behavioural reality (in this sense, pathology, as a normative concept, precedes physiology, as a naturalistic concept). But these ideas of suffering and death cannot be formed apart from the interpretation of the reports and the conduct of other people with whom one is in personal and social interaction. In this sense, the scientific-reductionist or atomistic-biological notion of diseased cells or organs depends on the holistic-clinical or holistic-humanistic conception of the illnesses of human persons.

Finally, as far as the functioning of the immune system is recalled, a high fever is anything but a state of subjective well-being, but the fact remains that even in this case symptoms may be considered as expressions of good health. With Canguilhem, one might say that "anomaly" (coming from a Greek word meaning "irregular", "uneven", "rugged") is not "abnormality". Physicians are worried about "anergic" patients, unable to increase their temperature when needed. Fever may be welcome whenever we know that it may be designed to preserve the patient's health as subjective well-being, and the ability to pursue the fundamental goals of their life, including survival.

2.5 Disease Is Not Enough for a Human Science; Nor Is Illness

So far, we have seen the difficulties inherent to the objective biological conception of malady as disease. At first glance, these difficulties might seem to point in the direction of a more normative and socially conditioned concept of health. As we have already mentioned, many attempts in recent decades to move in the direction of a holistic-humanistic perspective of malady are based on the concept of an ability to act in such a way as to enable the attainment of one's goals. For example, health can be defined as an equilibrium between personal capacities, social environment, and a person's "high-ranking projects in the life-plan" (Pörn, 1984, 1993), or a person's "vital goals" (Nordenfelt, 1984; see also Nordenfelt, 1986, 1995, 1997a, 1997b; Engelhardt, 1975 and 1984; Whitbeck 1981a, 1981b). Given that projects and goals are predicates of the person as a whole—and not of isolated molecules, cells or organs—, these theories of health, as already mentioned, are regarded as "holistic-humanistic", rivals to "atomistic-biological" ones.

However, on closer inspection, even a holistic-humanistic and culturally oriented

conception of health and malady lends itself to serious objections. Paradoxically, one could even say that certain aspects of a cultural conception of health and malady, which privilege it over naturalistic accounts, also constitute a weakness. If one admits that health and malady only depend on historically changing cultural values, they seem to lose all scientific relevance. In other words, if one admits that a patient's attitude towards their own disease frequently influences the success of the therapy to such an extent that a biological therapy itself becomes ancillary if not useless, the fundamental pillar of any objective control of the procedures that medicine uses to reliably treat patients falls. Moreover, this variability is increased by other problems that have their origin in what distinguishes the human sciences (or even the 'humanities') from the natural sciences, the "soft" from the "hard" sciences, that is, in the mediation by human consciousness.

Patients can report symptoms or present with behaviours unsupported by biological alterations, e.g., reflecting malingering or unconscious somatisations. These represent a severe challenge, mostly because the wealth of modern instrumental diagnostics inflates the risk of false positives for a known "disease". In other cases, the therapy could be prejudiced by the patient's knowledge of it. The widespread knowledge of psychoanalytic theory, for example, could be a great obstacle to this form of therapy, for patients can use it to reinforce their resistance to the unveiling of their actual unconscious motives.⁸ Surely, one seeks to obviate this problem by control groups and double, or even triple blind experiments, where neither physician nor patient (nor the researcher who evaluates the results) know who gets what. Yet, no matter what degree of sophistication one's methods of experimental control attain, the placebo effect will always interfere to some degree with the effectiveness of a treatment (on the difficulties of a definition of placebo, see e.g., Howick, 2016; for technicalities, see Benedetti, 2021). Faith-healing through pilgrimages has long been recognized by medicine as effecting unexplained recovery from somatic manifestations of psychological illnesses (Charcot, 1892). On the other side of the same coin, cases have long been recognized in which illness or even death may follow curses, an extreme variant of the so-called nocebo effect (Cannon, 1942).

All this is a serious weakness in the holistic-humanistic conception of malady.

⁸ See Legrand (1975). The psychiatric disorders leading to various clinical conditions, sometimes very severe, sometimes mimicking familiar diseases or impairments, and sometimes rather weird, have been variously defined since the first distinction between malingering and "hysteria" made by Jean-Martin Charcot in 1890 (Harris 2005). From the Freudian concept of symptoms representing a "conversion" of unconscious conflicts to the contemporary concept of semi-organic, "neuro-functional" disorders (Demartini et al., 2016), the pendulum never ceased to swing between a psychological and a neurologic interpretation.

No doubt, we need an objective, intersubjectively verifiable, socially (and perhaps legally) recognized concept of health. But given the important and unavoidable point made by the holistic-cultural perspective about health and malady, on what basis can we assert that a person is healthy or unhealthy in some intersubjectively testable sense?

The opposition of the two views about health and malady seems to end in an antinomy without any way out. The holistic-humanistic perspective apparently could, on one hand, show the naturalistic notion of disease to be untenable because it is unavoidably value-laden; but on the other hand, the demand for culturally changing decisions, values and norms seems to deprive the notions of health and illness of any genuinely scientific value.

2.6 A Recent Attempt to Heal the Old Gap

A recent debate has refreshed the illness-disease antinomy. The debate originated from a concern about the symptom of central fatigue, i.e., fatigue unrelated to exercise. This symptom is a common component of many illnesses, among which is chronic fatigue syndrome (which, embracing the “somatic” perspective, is also called myalgic encephalomyelitis). On the one hand, discussing this concept, Sharpe and Greco (2019) insisted on the possibility of an “illness without disease”. This is a concept whose validity is repeatedly admitted in the literature. For example, Hofmann (2017) notes, “there are no necessary connections” among disease, illness, and sickness, any of which, though *de facto* often occurring jointly, may perfectly well “occur without the others” (Hofmann, 2017: 18).

On the other hand, Wilshire and Ward (2020) claimed that the notion of ‘illness without disease’ is methodologically problematic and accused Sharpe and Greco of using the distinction between illness and disease “to identify a problem space that is not amenable to medical interventions at all, but rather must be addressed through social and/or psychologically based interventions”. The notion of “illness without disease” “can lead to unwarranted causal assumptions” as it seems to assume that “any experience not directly predicted by a disease model is necessarily of psychosocial origin” (Wilshire & Ward, 2020: 532; for more details on this debate, see Tesio & Buzzoni, 2020).

It might be objected that Wilshire and Ward’s criticism of Sharpe and Greco glosses over several important distinctions. In particular, instead of thinking of illness and disease “in terms of the hierarchical difference between subjective (or mental) and objective (or physical) realities,” Sharpe and Greco “propose that we could think of them in terms of different degrees and forms of abstraction from the totality of what is real.” (Sharpe & Greco, 2019: 185) However, though one may accept that both the experience of illness and what is usually called disease are “abstractions”, it is still necessary to raise the question about the

nature of the relationship between such abstractions as well as between them and the rest of reality: how are such abstractions connected with one another? And how can their connection be investigated in an intersubjectively reproducible and testable way?

Precise answers to these questions will be sought in vain in Sharpe and Greco's paper. In order to fill this gap they ought to provide a clear view about the causal relationship that exists between the different results of our abstractions, and especially between, on the one hand, the experience of "illness", and on the other, that aspect of reality which is the organic correlate of what is usually referred to as "disease" (and it goes without saying that if we do not wish to forsake science for magic and fiction, then this causal relationship should be such that, at least in principle, it can be made the object of an intersubjectively testable investigation).

On the other hand, however, Wilshire and Ward cannot accommodate one of the most important claims made by Sharpe and Greco, namely, that what is usually designated as the subjective, or better, normative-humanistic, dimension of health is relatively autonomous. Experiences of illness are real as long as they are 'lived through': in this sense, illness cannot be understood adequately only in terms, for example, of biological mechanisms, even if it is always possible to find some biological mechanism (at least some neural electric or metabolic activity) that is related to it and can be the subject of scientific investigation.

2.7 Healing the Gap by Rethinking Causality

Now, a first necessary step to answer this question in a satisfactory way is a more flexible, context- or perspective-oriented conception of causality. It is an important step, since it allows a psychological factor to be the cause of another psychological or even biological factor, and vice versa, rather than only speaking in terms of organic causes. To claim that this (bi-directional) interaction is not possible would be contrary to available evidence. It is a well-known fact that 'subjective' states can influence biological features, and this influence can be more or less direct. In the more direct version, it could take the form of changed biological parameters. For instance, 'stress' (admittedly a form of 'illness') can cause detectable changes in blood steroid concentration and immune markers (for a review, see Yaribeygi et al., 2017). In other cases, the influence of 'illnesses without disease' on the purely biological aspect of malady can be mediated by the personal, behavioural, and social context; for instance, depression appears to be more a cause than an effect of adolescent obesity, a condition associated with a broad series of related diseases.⁹

⁹ See Byrne et al. (2015). From this point of view, O'Leary's idea that a nonreductive dualism requires a clear distinction between "psychiatric care" and "medical care" is

It is important to stress that no direction of the causal vector should be privileged a priori. Instead, it can only be determined following experimental evidence. The experience of illness is a real thing that manifests within, and interacts with, the context of human existence. On the one hand, we see that there are decisive causal chains that go from the molecular to the cellular level to processes at the tissue level, which in turn are causally related to processes at the organ level, which again influence processes at the perceptual, behavioural, psychological and social level. On the other hand, however, in other circumstances and thanks to other pragmatic interests, we can see that processes at the biochemical level of cells are causally conditioned by processes at the tissue or organ level (see e.g., the “Tissue Organization Field Theory” of carcinogenesis developed by Soto & Sonnenschein, 2004, 2006, 2011), which in turn may be influenced by those at the interpersonal and social level.

Identifying the chemical or electrophysiological correlates of a psychiatric ‘disorder’ can be of fundamental therapeutic importance, but the possibility that words (which modify biological correlates) may be an essential ingredient of a therapy can never be excluded. The importance of observation and experiment should not make us forget that to cast aside the use of the spoken word in medicine was a unilateral, although perhaps historically necessary choice, which Virgil famously expressed by his definition of medicine as “the silent art” (*muta ars*).¹⁰

In this sense, the concept of illness encompasses the “pathology” not only of “psychologically-intangible” entities like feelings, emotions, and perceptions, but also of any observable behaviour that can be ascribed to a person as a whole. (By the way, there are no psychological states we can know, if not manifested through motor behaviour: consider, at a minimum, the blinking

untenable. It can be dangerous to provide only psychiatric care to patients in need of medical care (O’Leary 2020), but also to provide *only* medical care to patients in need of additional psychiatric care. By “psychiatric”, here, it is intended any form of “words only”, relational treatment, from psychological counselling to formal psychoanalytic approaches. O’Leary’s nonreductive dualism, as in the case of Wilshire and Ward (2020), also seems to lack a contextual and pragmatic conception of causality, i.e., one which does not limit a priori the directions of the causal vector. If we change the point of view and the interests of the investigation, it is in principle possible to trace a clinical picture back to causal links that refer, in different proportions to both biological and cultural reality.

¹⁰ On this aspect of the history of Western Medicine, see Laín Entralgo (1970: xxi). A word of caution is in order, however. Care must be taken in avoiding extreme reliance on “word-based” medical approaches, at the expenses of biological approaches. For instance, the interesting proposal of “narrative Medicine” (Charon, 2006) should not be embraced uncritically. In any case, it must be left to experimental science deciding to which ring of the causal chain the available treatments can be optimally applied.

eye of dramatic “locked-in” syndromes). Any form of disability is, actually, a form of illness: it is “lived through” by the person. A unidirectional bottom-up view of causality may distort the interpretation of behavioural results associated with biological treatments. For example, electrostimulation of the spinal cord has been claimed to allow the recovery of autonomous walking (with the help of rollators or parallel bars) in some chronic spinal cord injured patients (Angeli et al., 2014). It was objected, however, that learning a skillful use of the upper limbs might foster the transmission of force to the lower limbs, thus eliciting proper muscular reflexes (Tesio & Scarano, 2021): learning is a property of the person, not of the spinal cord.

2.8 An Open Challenge: Intersubjective Control

This viewpoint solves the problem of the possibility of causal influences between different levels of biological organization and in an important sense returns to the point of view of common sense. However, as we have just mentioned, this still does not solve the problem of intersubjective controllability which afflicts cultural conceptions of health and malady. There is no doubt that, if diagnosis and assessment of potential treatments are to be based only on the symptoms explicitly felt by the patients, or on their overall behaviour, or on the aims that they set themselves, or say they set themselves, they would be very variable, to the point of escaping generalisation and intersubjective controllability. To this should be added that malady is not something we can establish completely on our own, as isolated individuals, but always involves a social element. As noted by Talcott Parsons, illness may legitimately be regarded as a type of deviant behaviour (see the above comment on disability) which involves a particular social role: it is a claim upon others to be “taken care of” and relieves one of blame, shame and of certain social obligations, but it imposes duties to seek therapy from experts (Parsons, 1951: 283–297). Now, this dependence on the social recognition of malady by the community is also a factor of relativity, which must be somehow reconciled with the intersubjectively controllable nature of formal medical assessment.

Some authors have attempted to resolve this problem with an eclectic position, conceding something to the opposite perspective. In the next section, we shall briefly examine one of the most important attempts to develop a hybrid model of disease, that of Jerome C. Wakefield’s “harmful dysfunction model”.

3. Wakefield’s “Harmful Dysfunction Model” of Health and Disease. A Way Out?

3.1 Against the Nurture-Nature Dichotomy

According to Wakefield’s model, originally developed for mental disorders but

then generalised to all types of medically treated conditions, two requirements have to be met in order for something to count as a disorder: (1) an (evolutionarily determined) objective biological failure or dysfunction of an organ or body part has occurred; and (2) the dysfunction must cause a particular social harm (Wakefield, 1992: 3, 2007: 149–156; Wakefield, 2014; Wakefield, 2015).¹¹

Even in the case of Wakefield's model it can be said that, paradoxically, its greatest value is also its greatest weakness. It tries to integrate into a single model both the objective-organic and the interpersonal and social dimensions of malady, but because of its eclecticism, it is ultimately exposed to the objections that both parties raise one against the other.

On the one hand, the strength of this model lies in the fact that Wakefield makes every effort not to hypostatize the distinction between the natural and cultural spheres:

the contemporary understanding of brain plasticity means there is plenty of room for socially sculpted neurobiological changes not only since antiquity, but locally. The understanding of normality and pathology is [...] necessarily an understanding of the dance between evolved human nature and cultural influences. Moreover, evolutionary accounts are not limited to genetic and brain-matter levels. Thoughts and emotions are as biologically real as genes and neurons and have naturally selected features that operate at the representational level. (Wakefield, 2015: 351)

In the endeavour to overcome the nurture-nature (or the genes-environment) dichotomy, Wakefield is more and more supported by the growing evidence that acquired phenotypes (including behaviours and competences) can indeed be transmitted through “epigenetic” mechanisms working much faster than foreseen by the classic Darwinian paradigm (see on this, e.g., Crews et al., 2014, and Jablonka & Lamb, 2014).

On the other hand, however, he fails to answer satisfactorily the question of when a social change leads to a disease in the properly medical sense. His answer is that,

[w]hen culture exploits human variability and malleability—mental or physical—to sculpt human beings in socially desired ways, [...] the socially desired result is not a disorder if there is no socially defined harm. (Wakefield, 2015: 352)

¹¹ It should be noted that to some extent the main idea of Wakefield's model was anticipated by Robert M. Veatch, who also argued that health should be defined as “an organic condition of the body judged by the social system of meaning and value to be good.” (Veatch 1973: 78).

It is clear that this only shifts the problem without solving it: we do not yet have a criterion to distinguish between health and disease, because we do not yet know how to distinguish between the changes of human beings that involve and those that do not involve social harm.

Wakefield therefore tries to identify such a criterion, which he believes he has found in overly rapid social changes, which do not allow for the evolutionary adaptation of human cognitive structures:

the construction process can be pursued so relentlessly that damaging side effects occur that constitute true disorders. For example, the chronic stress of contemporary competitive educational and occupational environments that wring as much productivity as possible from the naturally talented can cause anxiety disorders in the vulnerable. Castel's characterization of at least some standard OCD [*sc.*: obsessive-compulsive disorder] cases would presumably fit here as genuinely disordered casualties of autonomy training. (Wakefield, 2015: 352)

As we can see, what causes the disorder is the fact that cultural evolution affecting biological structures does so much faster than the subsequent biological adaptation process, which, so to speak, cannot keep pace. But the criterion is clearly unsatisfactory. How can we distinguish between changes that are too rapid from those that are not? The only criterion here seems to be the emergence of a social harm, without which no health problems arise. A vicious circle seems evident.

Moreover, Wakefield rightly wants us to distinguish between correct and incorrect assessments of social harm: psychiatry becomes an oppressive social control if one incorrectly labels socially valued outcomes as natural and then classifies variations that fail to manifest the socially desirable features as disorders (see the above example of 'drapetomania') (Wakefield, 2015: 353). But this, on reflection, shows that it is only a value judgement that ultimately determines what we consider or do not consider a disease and, secondly, that biological modifications induced by a different cultural environment can and sometimes must be practically encouraged or, on the contrary, rejected and fought against.¹²

From this point of view, all the difficulties mentioned above regarding a normative

¹² Deformities resulting from binding of women's feet (Chan, 1970) and children emasculation to obtain castrati singers (Hatzinger et al., 2012) were not considered social harms for many centuries, before these practices were formally banned. The same holds for female genital mutilation, which is still widely practiced in various socio-cultural contexts (see: <https://www.unwomen.org/en/digital-library/publications/2020/07/a-75-279-sg-report-female-genital-mutilation>, accessed Dec 28 2021).

and cultural notion of what health and malady are, remain. Wakefield's model, in fact, does not tell us how it is possible to limit the problematic factors that undermine any attempt to establish in an intersubjectively controllable way whether something produces an authentic or only apparent "social harm". The difficulty is not gotten rid of, but merely shelved.

3.2 Opening a Crack in the Vicious Circle: Margolis's Model

An interesting variant of hybrid models of disease, which has not been discussed in the literature as much as its theoretical depth would warrant, was developed by Joseph Margolis. He rightly insisted that distinctions are smaller than they might seem at first glance: since the human body has changed over millennia relatively little as compared with social institutions, "the functional norms of somatic medicine are relatively conservative (unlike the norms of law)" because they are intimately connected with fundamental human abilities (Margolis, 1976: 575).

This model admits that one cannot speak of health or illness/disease unless one assumes the existence of fundamental objectives of human life with respect to which the functioning or non-functioning of our organism is a necessary condition. But in this model the achievement of these fundamental objectives requires, in a fairly uniform way, in the various societies, the possession of certain skills related to the use of our body in the environment in which we live, which would explain the relatively transcultural and ahistorical value of certain pathologies: the use of the hands to grasp objects and intervene for a thousand different reasons on the environment that surrounds us is so important that hardly an injury, deterioration or decrease in the functionality of our hands will not be considered as pathologic, and supported as a disease in all societies, across all ages.

Now, one can object to this position that the uniformity we are talking about is, in fact, only prevalently transcultural and ahistorical. Strictly speaking, there is no natural mechanism (be it physical, biological, chemical, etc.) that is not immersed in a cultural dimension that changes it in various ways. And it is always with an implicit or explicit reference to this cultural mediation that we can speak of health and malady in humans. Take the example of the difficulty or incapacity to read (dyslexia), clearly a neural biological problem, which could be detected and named a "disorder" only in a social context where some literacy is expected from the population: in fact, it was "discovered" in Germany, only in 1887.¹³

¹³ For a history of dyslexia, "both an ongoing psychological diagnosis and a social construct", see <https://dyslexiahistory.web.ox.ac.uk/brief-history-dyslexia>, accessed Dec 28th 2021.

To sum up, despite some biological constraints, health remains largely relative to persons, to their interpersonal and societal environment, to a meaningful relation with it, to custom, and convention. And it is precisely this measure of wide variability that raises the problem of the intersubjective controllability of our judgements about health and malady in different societies and in different historical periods. Moreover, as Engel never tired of pointing out, social values do not merely infuse the appraisal of biological dysfunctions, but they also infuse the various and individual ways that one responds to those dysfunctions (Engel, 1960, e.g., pp. 466–467). We seem to have fallen back again into the antinomy highlighted already in Sect. 2.

As we shall see in the next section, in order to solve this problem satisfactorily—in addition to a pragmatic and contextual theory of causality, which we cannot dwell on here (see in particular Buzzoni, 2014 and Tesio & Buzzoni, 2021)—it is necessary not only to allow that illness, in some cases, can powerfully influence its organic basis (and therefore the “disease”), but also to understand how this interaction is not arbitrary, but responds to regularities which, although different from those of the natural sciences and proper instead to human sciences, can be ascertained in an intersubjectively controllable way.

4. Medicine as a Human Science

4.1 *Human Sciences: Habits as Law-Like Regularities*

Everything we have said so far about the cultural aspect of health and malady seems to suggest that it is impossible to satisfy one of the basic prerequisites of any empirical and scientific notion, namely that of being intersubjectively controllable. The problem now is: How far, and in what form, is it possible to reconcile the unpredictable variability of the way in which the individual patient or particular groups of patients experience their health and illness with the equally undeniable organic-objective basis of their lives (and whose importance lies at the basis of the very notion of “disease” as opposed to illness). It has already been hinted that the answer to this question lies, at least to some extent, in the answer to another question: In what sense, and to what extent, is medicine a “human science”? As already mentioned, the term human should not be taken as a synonym for “humanitarian”, but in the more classical sense instead, meaning a science that studies the ways in which human beings (classified as *Homo sapiens sapiens*), throughout their history, manifest themselves in various ways of coping with the natural and social environment.

Now, the answer to the question just raised (and the justification of our claim about the unity and distinction between analytical and holistic perspectives) can only be satisfactorily given if a fundamental characteristic of medicine, which it shares with other human sciences (such as psychology, sociology and, as a borderline case, historiography itself) is brought to light. This is not the place to

give a comprehensive outline of the epistemological and methodological status of the human sciences. But we do want to insist on a point without which the link defended here between unity and distinction, and between the analytical and holistic perspectives on health and disease would remain suspended in the void, and specifically, without philosophical justification (for a more adequate justification of the brief hints that follow, see Buzzoni, 1989, 2010).

The subject matter of the human sciences is the result of a peculiar process of sedimentation of that which was wanted or done in the past by human beings. Typical focii include habits concerning action and thinking established by frequent repetition, more or less consciously transmitted to descendants. Human relationships are based on a more or less unconscious tissue of habits, regarding acting or thinking conditions both at the individual and the collective level. These habits are quasi-mechanisms on which institutions, traditions and customs are based, or, to put it another way, usually we follow these habits quasi-mechanically and unconsciously, for which reason they are very difficult to avoid. The regularity and predictability of human habit grounds talk of the “bureaucratic (mega)machine”, the “machinery of justice”, the “market machinery”, and the like. More precisely, human actions depart mostly to a negligible extent from these habits, so that one is able to subsume such actions under general—psychological, sociological, etc.—law-like regularities in order to explain them.

While, in this respect, the rules concerning human actions are analogous to the scientific laws of nature, they can at any time be revoked by becoming aware of them. This makes it possible for human beings to modify, improve or sometimes even entirely (or better, almost entirely) suspend or change psychological, sociological, ethnological, medical, etc., regularities. Psychoanalysis is paradigmatic of this, but everyday life also repeatedly confirms the possibility of suspending routines as fixed ways of thinking or doing things. By contrast, you can change a Ptolemaic model of astronomy in favour of a Copernican one, but no change of attitude can suspend the relative Sun-Earth motion itself.

In other words, human actions always have two sides. One side consists largely of unconscious routines and quasi-automatisms governed by law-like regularities or rules, and this allows a scientific explanation of human actions; the other side persistently dissolves the routines or quasi-automatisms in new courses of action. The two sides are not separate, but dialectically connected. Far from being inconsistent with one another, each of the sides presupposes the other, and each is necessary for the appropriate interpretation of the other: the possibility in principle of suspending (relatively) unconscious rules or habits is indeed the other side of a de facto dependence of our will on these rules or habits, without which, on reflection, no free action would be possible.

Now, if we apply these considerations to the above theses regarding the relationship between the analytical-reductionist and the holistic-humanistic perspective on health and malady, as well as the relationship between “illness” and “disease”, we are in a position to identify an important, but usually neglected characteristic of medicine as a human science.

4.2 Why Medicine Can Be a Science

As we have sketched above, the cultural dimension of human actions consists to a very great extent in unconscious, law-like habits, and this makes it possible to recognise intersubjectively testable connections not only between some symptoms and some objectively ascertainable processes in the ill body, but also in the various, individual as well as collective ways to respond to illness (as the lived experience of bodily and mentally painful and/or disabling processes) and to the often, but not always, diagnosed disease (and thus to the associated statistics and/or organic dysfunctions). The powerful influences exerted by the cultural, subjective-interpersonal and social, dimension on the organic dimension of malady and health are not arbitrary; on the contrary, they obey laws which, even though different from natural or empirical laws (because they are made, accepted, modified, or rejected by human beings), they are sufficiently stable to make possible predictions and explanations similar to those of the experimental sciences. For example, on the one side, dyslexia would not be a medical problem in an imaginary future society where information might be transmitted electronically from brain to brain with no mediation of written words. But in spite of the fact that perhaps reading will not be a human task in a science fictional future, dyslexia will likely be considered a medical problem deserving a rigorous scientific approach for many generations to come.

From this point of view, if we define illness as the lived experience of bodily and mentally unwanted painful and/or disabling processes, medicine must be concerned with more than “diseases” and “illness” in the most common (for example in Boorse’s) sense. Medicine must also be explicitly concerned with *the more or less law-like ways in which patients as persons (as well as the members of their families or wider social environment) respond to illness and disease*. In other words, not only illness as the lived experience of bodily and mental processes, such as respiratory wheezes, abdominal cramps, painful joints, and stuffed sinuses (see e.g., Kleinman, 1988: 3–4), but also the law-like attitudes of patients about how best to deal with illness (in its wider sense, including disabilities) and with the associated practical problems in daily living. To the extent that the illness and disease, as well as their classifications, depends upon such attitudes and reciprocal expectations (and upon conventions, policies, social norms and roles constituted by those attitudes and expectations), they should be studied as part of the genuine subject-matter of medicine as a human science, with the technical specificities that this nature

requires.

4.3 The Specificity of a Human Science

The cultural influences on illnesses and diseases (as well as on their classifications) we have stressed in the preceding section do not exclude the possibility of formulating law-like regularities concerning the object of medicine. However, they impose some methodological precautions and constraints. As already mentioned, while in one sense the rules concerning human actions are analogous to the scientific laws of nature, in another sense they differ in principle from them, because they can at any time—in principle entirely, but de facto only to some extent—be suspended by any individual becoming aware of them (this possibility is confirmed not only by psychoanalytic and neuroscientific inquires into tacit knowledge, but also by our everyday experience).

The methodological counterbalance of this possibility that is typically used in the humanities is, so to speak, a second-level use of the statistical tool, which is of interest here only insofar as it depends on reasons other than those for which statistics has been adopted in the natural sciences. In fact, the conventional bio-statistics aimed at summarizing data and making inferences on the observed measures may be regarded as a ‘first-level’ strategy: necessary, but not sufficient, in the human sciences (including medicine). The further second-level, here, includes two peculiarities:

- a) the need for a circular statistical approach moving from individuals to populations and vice versa, and
- b) the need for statistical inference on the nature of the variable under study.

The biological effect of an intervention (e.g., a given drug) interacts with the socially-influenced, yet highly individual, subject’s psychology. Consistently enough, drug research necessarily requires experimentation on humans. Of course, tests on humans are needed because biological specificities must be taken into account. Another reason, however, and of more interest here, is that the person’s variables must be taken into account: they converge in determining effect modifiers such as treatment compliance, life habits, proneness to the placebo effect, and the like. Trial designs, therefore, should include such variables, which are of little to no use in studies on animals. One may object that individual peculiarities, both biological and behavioural, can be conditioned out through proper use of population statistics (e.g., the placebo effect can be neutralized by randomisation to the treatment and placebo arms of the study), thus making research practice on humans similar to practice in the natural sciences. However, statistics on data (e.g., means, standard deviations, etc.) wipe out fundamental information on the reasons

why individual responses did vary: a critical flaw given that as a rule clinicians treat single cases. For this reason, medicine needs statistical methods to estimate what is the degree of uncertainty (modelled as error) surrounding single measurements and their changes in individuals: an uncertainty-error typically larger than that affecting population means (see Tesio, 2012a). Whereas statistics on forces and temperatures can give us a glimpse into the nature of the variable, the same does not hold, for instance, for statistics on “depression”, “quality of life”, “pain”, “balance” and the like: for an investigation into the existence and nature of these requires a “second-level” of inference.

The necessity for all human sciences (including medicine) to resort to specific statistics is not the result of overly complex subject matters. In other words, it is not due to some unavoidable ignorance of all the relevant factors and the relations between them (as is usually the case in the natural sciences). Rather, the necessity results from something intrinsically connected to the nature of the human sciences’ subject matter: one must resort to statistics because one cannot abstract entirely from personal consciousness, which is a relevant causal factor unknown *per definitionem*. Since the rules we find in the human sciences can change or dissolve, these sciences, including medicine, are under an obligation to inspect constantly the validity of the rules on which their predictions and explanations are based, both by indirect, statistical, and direct, clinical-empirical methods. The statistical approach is, as it were, the best available counterweight to the risk, which always hangs over the human sciences, of investigating the ‘wrong’ subject-matter, a subject-matter that could at any time change because it is partially self-made, and therefore escapes the generalisations so far successfully applied to it. The particular character of the “laws” of the human sciences in general is thus closely connected to the duty of these disciplines to test and support their assertions not only directly, with reference to particular cases, but also indirectly, by means of specific statistics. It should be clear that the issue of statistics is of critical relevance to our discourse, so that a digression is needed.

5. Replicating the Illness/Disease Dichotomy: Statistics from Biology to Behaviour

It may be useful to recall that nowadays, by “statistics”, two wide domains of human knowledge are intended. Boldly stated, the first includes the algebraic techniques used to describe, summarize, or predict some measures and their uncertainty (descriptive and inferential statistics, respectively). The second domain includes the logic of the experimental set-up, fostering reliable inferences about the causal rather than the merely associative nature of the relationships across variables (“trial design”, in medical jargon). For instance, computing means and tracing a regression line are algebraic; adopting a double-blind protocol is an essential component of trial design. Looking at the

algebra, it must be noticed that Claude Bernard, the founder of contemporary “experimental” medicine (see e.g., Bernard, 1865), did not like inferential statistics (already highly developed at his time). He saw biological processes as deterministic (after all, they were seen as results of chemical/physical phenomena), so that the predictions allowed by authentic laws should be free from uncertainty. He conceived the deviance of observed results from expected ones (paradoxically) as the effect of imperfections in the experiments and/or the assumed law of nature. To many contemporary clinicians, algebraic statistics still appear as a sort of complicated cosmetic surgery done to embellish imperfect data, or to over-simplify empirical reality.¹⁴ The alarm has been raised that “in medicine today uncertainty is generally suppressed and ignored, consciously and subconsciously” (Simpkin & Schwartzstein, 2016). Uncertainty in medicine has been the topic of philosophical discourse (Djulbegovic et al., 2011), and of proposals for new training regimens for medical students (Tonelli & Ross Upshur, 2019).

The problem cannot be solved as long as two key points are overlooked.

First, biological statistics, the one (scarcely, indeed) taught to clinicians, is based on population summaries (e.g., means or medians) whereas clinical practice faces single and entire, much less predictable, individuals.¹⁵

Second, whole-person variables are much less regular (i.e., there are more peculiarities/idiosyncrasies), compared to biological variables, for the reasons expressed above. To overcome this difficulty, in the early twentieth century, psychology married statistics and generated a branch now called “psychometrics”, although the word “personmetrics” might be more appropriate (Tesio, 2003). Psychometrics, in turn, coined the term “latent variables” (or latent traits) to indicate variables (such as perceptions, abilities, attitudes) than can be ascribed to a whole person, only. These variables have an inherent variability-instability, within and between subjects, going beyond the variability caused by both

¹⁴ Statistical verbiage does not help. The word “regression” has a disagreeable flavour, although it defines perhaps the most popular procedure. By “regressing” the data you lose dimensions: points dispersed in a volume can be regressed to a plane; point dispersed in a plane can be regressed to a line. Means and medians themselves are a form of regression: you lose a line and obtain a point. The statistical language of uncertainty is no more reassuring: “standard error”, “confidence limits”, “hypothesis testing”, all apparently point towards unavoidable approximation in attaining scientific “truth”.

¹⁵ It may look paradoxical that both chemistry, physics and biology on the one side, and epidemiology, on the other side, deal with abstract “mean” entities, be they molecules, cells or citizens. Individual differences are managed as sources of “variance” with respect to the primary object of study, using more or less the same statistical principles (see Tesio2019). By contrast, single persons are the object of clinical practice. Applying to persons the same experimental paradigms valid for electrons and elections may be highly misleading. Renouncing any statistical control, however, confines observations in the limbo of anecdotes.

biological instability and measurement errors, and related to the “interaction between person and situation” (Steyer et al., 1999). Boldly stated, “noises” of both biological and relational origin interact in the manifestations of such variables. Pain, depression, memory, language, continence, balance, voluntary force, fatigue, all may manifest themselves in potentially infinite circumstances, and with variable intensity. These properties are much more indirectly observable than body weight, nerve conduction velocity, or glucose concentration, and inferences must be done on a very limited set of observations, usually lumped together in cumulative questionnaires. These provide scores that simply report counts of observations (e.g., how many yes or no answers one gives to questions listed in a questionnaire).

How much of the latent variable is represented by “yes = 1” to different questions is unknown, so that models are required to infer true linear measures from the so-called raw scores. Uncertainty is increased by the fact that the very existence of the “latent” variables is debatable: there is always the risk that we are cramming into the questionnaire items that just reflect the author’s opinion (if not prejudice), so that the variable is imagined rather than discovered (items “form” rather than “reflect” the latent variable, according to the psychometric jargon). This ontological problem thus adds to the problem of quantitative estimation (Borsboom et al., 2003).

The trial design also requires a particular approach. The armamentarium typical for biological research (e.g., randomization to “true” vs “control/placebo” treatment; double blind treatment/assessment) does not fit the individual, customized, multifactorial and relational (in short: clinical) approach to illness.

All of the above peculiarities, however, represent technicalities and not ontologically irreconcilable differences between a truly quantitative/experimental and a purely qualitative/descriptive approach. These problems are well known to the world of the so-called “soft” or “human” sciences (from psychology to education and marketing), and elegant formal solutions have been proposed that allow investigators to apply scientific rigour to both the algebra (e.g., Tesio, 2003) and the trial design of “statistics” (Shadish, Cook, & Campbell, 2002) in these fields of human knowledge. Simply put, medicine is eager to snub the know-how of the “soft sciences”, thus unnecessarily slowing down the possibility of scientific discovery in conditions where illness is just as relevant as (and often more accessible than) disease (Tesio, 2019). Measuring the effects of treatments in terms of both biological and behavioural changes, and in terms of number of patients changed rather than “mean” changes, may lead to more rational decisions (for an example, see Zamboni et al., 2018).

The illness standpoint on human suffering is prioritized by “alternative” /“complementary” forms of medicine. “Alternative” is the more adequate

adjective for those approaches that do not accept the link to contemporary experimental method (Tesio, 2012b). In so doing, they free the treatment of illness from any formal obligations with respect to the treatment of disease. Not surprisingly, “alternative” medicine is rising in popularity, whereas “alternative” biology, physics, chemistry, if they exist at all, are much less popular.

6. Reconciling Individual Observations and Statistics

6.1 The Circle of Extraclinical and Clinical Knowledge

We can now better formulate the scope and limits of Boorse’s definition of disease. On the one hand, there is an element of truth in his insistence on the use of statistics in the definition of the concepts of disease and health. As we have said, the dependence in principle of any general ‘rules’ on the consciousness of the individual patient represents a factor of uncertainty that cannot be completely eliminated in medicine, insofar as it is a science of humans. In some cases, cultural and social variability will be minimal (when highly effective methods and instruments are found to solve problems related to the functions of our bodies that are fundamental in most cultural circumstances). In other cases, however, for example in the psychiatric context, it will usually be very difficult to minimize uncertainty (especially in cases of psychological features that are easily exposed to the influence of culture and political power). But in all cases this uncertainty can be (to varying degrees) limited by applying the appropriate statistical tools as a methodical counterweight, in order to ascertain that the conjectured rules are true of at least a significant number of individual cases (‘significant’ with respect to our purposes).

But, on the other hand, the converse is also true, and it brings to light the limits of Boorse’s naturalistic concept of disease. A definition of disease or health cannot be based on statistics and/or biology alone because it cannot be entirely separated from considerations of the overall behaviour, whether analytic or holistic, of the individuals to whom we wish to ascribe a state of health or disease. The main reason is simple. There is no human statistic that is not based on the interpretation of individual cases. The statistical test of the efficacy of a biological therapy cannot entirely take place without data obtained in the clinical setting by means of the clinical method, a vast domain in itself (Piantadosi, 2017), because one can ascertain only in the clinical encounter whether the patient’s change occurred or not. For example, *pace* Grünbaum (1984), to ascertain whether a single case of mental illness can be classed as a case of paranoia, one must presuppose a definition and an operationalization of ‘paranoia’ that is at least implicitly clinical (Buzzoni, 1989). Defining not only a “disease”, but also a “syndrome” or a “disorder” implies extracting regular associations of signs and symptoms from many single patients, in which different sets of signs and symptoms occur. Extraclinical tests can never

entirely free themselves from clinical ones. There are no statistics on human subjects that can leave aside an interpretative understanding of the single cases on which they must ultimately be grounded. A pathologist or a physiologist cannot even begin their research without presupposing the existence and at least the partial reliability of clinical results (a reliability, as we have pointed out, that is also based on the law-like connections that medicine shares with the other human sciences).

We come here to a general conclusion: even though there are many ways to reduce the subjective-cultural variability of a patient's behaviour and to measure appropriately the quantity of their "latent" traits, one must bear in mind that all of this must be in the end tested by resorting to single cases again, all of which are mediated and partially obfuscated by the presence of consciousness. The search for objective relations clashes with difficulties that one can always try to minimize, but never wholly eliminate. If, in a sense, the reliability of clinical tests presupposes the reliability of extraclinical tests, in another sense, extraclinical tests presuppose the reliability of clinical ones. Or, to put it another way, the growing success of population- and evidence-based medicine (Greenhalgh et al., 2014) is epistemologically and methodologically well-grounded, but only if one does not neglect that this approach, in an important sense, is inherently dependent on clinically-based evidence

6.2 Making Virtuous a Vicious Circle

Does the swinging from individual to statistical population means imply a vicious circle? The answer is no: not only from a hermeneutic, but also from an operational point of view, it is easy to acknowledge that there are not only vicious, but also virtuous circles, in which self-correcting or spiraliform procedures take place, with qualitatively new results, which each procedure alone could not produce. There is an obvious but important sense in which a reciprocal presupposing is not vicious. A circle is not operationally vicious if each of its elements (or actions)—even though similar in almost all respects—is different from at least one viewpoint. Such a difference makes it possible for each element to support the other (or others) in obtaining a novel effect, in a spiraliform progress. Everyday life offers plenty of examples. One cannot make a playing-card stand on a table in a slanted position, but this happens when one playing-card leans against another, and vice versa. For playing-cards (or the relative actions that are to be performed on them) are similar from many viewpoints, but are different at least with respect to their inclination at a particular time and place. In this sense, building a house of cards is a good example of procedures in which an action presupposes another action (and vice versa), and yet each action could not attain the intended result without the reciprocal one. The same organs (e.g., brain, muscles, sensory organs, etc.) can be studied from the perspective of their homeostatic biology within the body or, from the perspective of their capacity to provide the individual with active

interactions with the external world (Tesio, 2020). In a similar way, even though similar in many respects (both approaches aim at the maintenance or restoration of health of concrete people, both recognise experimental evidence as the ultimate criterion for the reliability of their statements, etc.), the analytic-reductionist perspective (based on biochemical or physical research and statistical analysis) and the holistic-humanistic perspective (based on clinical methods) are different from various viewpoints: they operate in different contexts, on different variables, give different importance to generalized truths and particular events, etc. More precisely, if on the one hand the analytical-naturalistic perspective on health and malady must be subordinated (so to speak ethically and ‘teleologically’) to the holistic-humanistic one, on the other hand the latter must be filled (so to speak ‘mechanistically’) with intersubjectively controllable empirical contents.

There is therefore no vicious circle in using clinical results to formulate statistics or in using laboratory values to correct the subjective-cultural elements that are involved in the maintenance or restoration of health. As one does not need a hammer to forge a hammer, so considerations about the illness of the patient and the ways they respond to it need not be definitively established in order to reinforce extraclinical (biochemical and statistical) considerations, and vice versa. They must only claim a provisional degree of certainty, tentatively assumed to acquire a further, additional one.¹⁶

6.3 Reconciling Singularities and Regularities

We have tried to show that the variability of individual clinical assessments is not unlimited. Even the clinical response of the individual patient can in reality never completely escape (and indeed is usually influenced by) factors exhibiting the same kind of regularity that is typical of the laws of the human sciences. The interpersonal-cultural dimension does not exert an arbitrary or unpredictable influence on the organic dimension of health and malady; on the contrary, its influence obeys regularities which (although different from the natural ones, because they are constantly modified by human beings) are sufficiently stable to make possible intersubjective statements about human health and all the concepts that are closely connected to it: prevention, diagnosis, prognosis, therapy, etc. Only by adding this piece does Wakefield’s

¹⁶ It is of interest that biostatistics is revitalizing the study of single cases as an important source of knowledge (Gabler et al., 2011), taking up a long tradition in psychometrics (Tesio, 2012a). Both in biostatistics and psychometrics, knowledge acquired from population studies may be fed back, through proper algorithms, into single-case designs. This creates a virtuous circle bridging the gap between the ‘scientific’ status of population studies and the merely anecdotal evidence of individual observations, which are so relevant in clinical practice. The issue has been expanded upon for the specific case of physical medicine and rehabilitation medicine in (Tesio, 2019).

position (see above, Sect. 3) become sustainable. It is only by adding this element that we can understand in what sense the “social harm” in Wakefield’s model of “harmful dysfunction” also possesses scientific and intersubjective value. Without this element, his position remains close to common sense, but it also remains hopelessly eclectic and insufficiently well-supported. The same holds for Canguilhem’s position: if any statement about “the normal and the pathological” is irremediably value-laden, medicine will never be a science. We contend that it can be, if essentially the same scientific method is applied to the person, though with the methodical corrections (and the proper modesty) made necessary by the different variables observed (i.e., behavioural-holistic vs biological-analytic).

From this point of view, the problems connected with the possibility of an intersubjectively controllable definition of health and malady are, at least in principle, solved: they do not necessarily make such a definition impossible, since it is possible to exploit regularities in contexts that are more strongly conditioned by the material-organic base, as well as in those that are more sensitive to cultural influence. Exploiting these regularities can guarantee a certain intersubjective controllability. How far this intersubjective controllability extends cannot be decided a priori. It is decided by the researcher (including the clinician himself), i.e., the scientist at work, when they give us reproducible and therefore intersubjectively controllable results in fields that until then have not yet been included in scientific knowledge, precisely because they lacked this fundamental property.

This makes it possible to limit to a great extent the uncertainty that is natural to the human sciences, although we must be aware that it can never be completely eliminated. No matter how sophisticated control methods become—to limit ourselves to what is perhaps the sharpest example—the placebo effect will always interfere to some extent with the therapeutic efficacy of a treatment. In the same vein, we cannot exclude a priori that certain antibiotics may have different effects with respect to certain social groups (and a fortiori with respect to particular patients) than those that have been shown in the populations where they have been used until now: which is because behavioural and social features are no less important than genetics. But just the awareness that medicine is a human science in the sense defended here may lead to concrete improvements for real medical practice, both clinical-individual and biomedical-statistical: what is called for is some awareness that we must establish from time to time if and how much the status of human science has or has not influenced our categorisations, diagnoses and therapies, and therefore in which direction we have to look for improvements both of biomedical knowledge and clinical practice.

7. Conclusion

In the literature of the last decades about the status of medicine, a new awareness has grown that an adequate notion of medical praxis requires an integrative position, which combines the analytic-reductionist with the normative-holistic perspectives on health and illness/disease. We have tried to show that it is possible to take an important step towards such an integrative view, if the relationship of unity and distinction between what we usually designate as 'illness' and 'disease' is correctly set up.

The demand for such an integrative view is a result not only of ethical considerations (which were not discussed here), but perhaps even more fundamentally for epistemological and methodological reasons, intimately connected with the status of medicine as a science of humans. In this connection, the key idea has been that the variability in the ways in which patients experience and respond to their illnesses— which is emphasized by the holistic-normative views about health and malady—is subject to regularities that may be investigated in an intersubjectively testable way. On the one hand, this variability—which originates in what distinguishes all human from natural sciences, that is, in the personal human consciousness on which all law-like relations of human and cultural reality depend in principle—undermines the scientificity, i.e., the intersubjective controllability, of medicine. On the other hand, however, this variability can be methodologically counterbalanced by the fact that the cultural domain of illness, like the objects of other human sciences, is subject to regularities that may be investigated in an intersubjectively testable way. Because these regularities add to, and may interfere with, those that biological research investigates, medicine cannot ignore its nature as a human science. It must be concerned not only with “diseases” and “illness” in the most common (for example in Boorse’s) sense, but also with the ways in which patients as persons (as well as the members of their families or wider social environment) respond to malady and associated practical problems in everyday life. Insofar as such attitudes and expectations (as well as conventions, policies, social norms and roles constituted by those attitudes and expectations) influence the criteria of illness (and disease), they must be studied as part of the genuine subject-matter of medicine as a science.

Although there is a factor of uncertainty that cannot be completely eliminated in medicine, insofar as it is a science of humans, this uncertainty can be (to varying degrees) limited by applying appropriate statistical tools as a methodical counter-weight, in order to ascertain that the conjectured rules are true of at least a significant number of individual cases ('significant' with respect to our purposes). In this connection, it is important to note that a definition of disease or health cannot be based on statistics and biology alone because it cannot be entirely separated from considerations of the overall behaviour, whether analytic or holistic, of the individuals to whom we wish to ascribe a state of health or disease. The main reason is that there is no human statistic that is not based on the interpretation of individual-clinical cases. The statistical test

of the efficacy of a biological therapy cannot entirely take place without data obtained in the clinical setting by means of the clinical method, because one can ascertain only in the clinical encounter whether the patient's change occurred or not. Extraclinical tests can never entirely free themselves from clinical ones. Even though there are many ways to reduce the subjective-cultural variability of a patient's behaviours (which are always also interpersonal and social answers to their illness or disability), and to measure appropriately the quantity of their "latent" traits, one must bear in mind that all this must be tested, in the end, by resorting to single cases, where the blurring mediation by consciousness reappears. The search for objective relations clashes with limits that one can always shift away from, but never wholly eliminate. It follows that the reliability of clinical tests presupposes the reliability of extraclinical tests, and extraclinical tests presuppose the reliability of clinical ones (and vice-versa); or, said otherwise, population- and evidence-based medicine is epistemologically and methodologically well-grounded only in its synergy with clinically based evidence.

Funding This work was supported by the Italian Ministry of Education, University and Research through the PRIN 2017 program "The Manifest Image and the Scientific Image" prot. 2017ZNNW7F_004 and by the Italian Ministry of Health, "ricerca corrente", Istituto Auxologico Italiano-IRCCS, RESET project).

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