The Journal of Medicine and Philosophy: A Forum for Bioethics and Philosophy of Medicine,
2024, **49**, 367–388
https://doi.org/10.1093/jmp/jhae017
Advance access publication 17 June 2024
Original Research

Wakefield's Harm-Based Critique of the Biostatistical Theory

CHRISTOPHER BOORSE*

University of Delaware, Newark, Delaware, USA

*Address correspondence to: Christopher Boorse, PhD, University of Delaware, 24 Kent Way, Newark, DE 19716, USA.
E-mail: cboorse@udel.edu

Jerome Wakefield criticizes my biostatistical analysis of the pathological—as statistically subnormal biological part-functional ability relative to species, sex, and age—for its lack of a harm clause. He first charges me with ignoring two general distinctions: biological versus medical pathology, and disease of a part versus disease of a whole organism. He then offers 10 counterexamples that, he says, are harmless dysfunctions but not medical disorders. Wakefield ends by arguing that we need a harm clause to explain American psychiatry's 1973 decision to declassify homosexuality. I reply, first, that his two distinctions are philosophic fantasies alien to medical usage, invented only to save his own harmful-dysfunction analysis (HDA) from a host of obvious counterexamples. In any case, they do not coincide with the harmless/harmful distinction. In reality, medicine admits countless chronic diseases that are, contrary to Wakefield, subclinical for most of their course, as well as many kinds of typically harmless skin pathology. As for his 10 counterexamples, no medical source he cites describes them as he does. I argue that none of his examples contradicts the biostatistical analysis: all either are not part-dysfunctions (situs inversus, incompetent sperm, normal-flora infection) or are indeed classified as medical disorders (donated kidney, Typhoid Mary's carrier status, latent tuberculosis or HIV, cherry angiomas). And if Wakefield's HDA fits psychiatry, the fact that it does not fit medicine casts doubt on psychiatry's status as a medical specialty.

KEYWORDS: *biostatistical theory, disease, DSM, harmful-dysfunction analysis, health, homosexuality, Jerome Wakefield, normal flora, pathology, psychiatry, situs inversus, subclinical disease, Typhoid Mary*

I. INTRODUCTION

Jerome Wakefield argues that his harmful-dysfunction analysis (HDA) better captures the concept of medical disorder than does my biostatistical theory (BST) in virtue of his requirement that disorders harm the individual.[1] He pursues this theme in two broad ways. One is to discuss my general claim that pathologists' usage of disease language is authoritative and my specific application of this claim to Nordenfelt's "one–dead-cell" objection. Wakefield finds my claim and reply deficient in failing to recognize two basic distinctions: (1) disease of a part versus disease of the organism, and (2) biological versus medical pathology. To illustrate these distinctions (which, he thinks, coincide) and to prove his point, he then offers, as counterexamples to the BST, what he believes to be 10 harmless dysfunctions that medicine does not classify as disorders. He concludes by explaining how the HDA, but not the BST, might approve Robert Spitzer's justification of the American Psychiatric Association's 1973 decision to normalize homosexuality: namely, that whether or not homosexuality involves biological dysfunction, it can be seen as harmless by "evolving social values" (Wakefield, 2014, 676).

In reply, I shall observe, first, that Wakefield's distinctions (1) and (2) do not serve his purpose, since his discussion of homosexuality and missing kidneys shows that they do not coincide

with the harmless/harmful distinction. In any case, these distinctions play no role in medical thought. They are philosophic fantasies alien to medical usage, invented merely for the purpose of saving the HDA from a host of clear counterexamples. There is no medical boundary between disease of a part and disease of the organism. All diagnoses are disorders of the individual, not just of a part, and any part-dysfunction can be given a disorder name. To illustrate these facts about medical terminology, I examine three chronic diseases—emphysema, type-1 diabetes mellitus, and coronary atherosclerosis (§III). Since these diseases are subclinical in the early stages, they also exemplify my distinction between theoretical and clinical health. In §V, I supplement subclinical disease with five examples of harmless skin disorders. As for Wakefield's 10 purported counterexamples (§IV), it is hard to generalize about them, except that no medical source whom he quotes describes them as he does. In each case, he rewrites his sources in his own vocabulary. I address the counterexamples in various ways, but often by distinguishing one disease from another.

Let me make some quick methodological remarks before beginning. Although, as Wakefield notes, I have said that I see pathologists' usage of terms like "disease" and "disorder" as fundamental, all my points in this essay can be made from clinical sources too. I cite textbooks and reference works not merely on pathology, but also on general medicine and its many specialties. Although I view these works as the best authorities on medical usage, an often-convenient shortcut is the World Health Organization's (1994) ICD-10 classification. But one must bear in mind this document's limitations. It is intended as a "practical," not a "purely theoretical," classification, mainly for record-keeping and statistical purposes.[2] It is natural to view an ICD-10 listing as sufficient for disorder status—though there is always the possibility of inaccurate classification, as Wakefield (2014) himself claims regarding situs inversus totalis. But ICD-10 listing cannot be viewed as necessary to disorder status, since pathological conditions only get listed if they play some role in medical practice, and there are many conditions familiar to pathologists that, for one reason or another, do not turn up in the clinical setting. Virtually by definition, subclinical disease never gets coded in ICD—but, as we shall see, that hardly shows it is not disease of the organism.

II. WAKEFIELD'S TWO DISTINCTIONS

At the outset, Wakefield quotes my 1987 paragraph in which I replaced "disease" in the traditional medical slogan "Health is the absence of disease" with the broader, more accurate term "pathological condition." I wrote:

> I suggest that the distinction between normal and pathological conditions is the basic theoretical concept of Western medicine. A bodily state is disease, disorder, injury, lesion, defect, sickness, or illness only if it is abnormal in the sense of pathological . . . [O]ne defines a medically ideal (and nonexistent) human being as one completely free of all pathological phenomena at every level of physiological function . . . (Boorse, 1987, 364–365)

Wakefield then considers my reply to a criticism of my account by Nordenfelt, who wrote:

> We shall then say [on the BST] that health obtains in the organism when all cells fulfill their functions. Otherwise there is at least one disease. The consequences of such a view are extremely counterintuitive. The existence of a single cell not fulfilling its functions is sufficient for the existence of disease and thereby the non-health of the whole person. We all have a great number of cells which are dying or malfunctioning. Hence, we would all be ill. (1987, 28)

My reply to Nordenfelt included the following:

> [T]o the pathologist no one is normal . . . One dead cell is just the ultimate in focal necrosis, one of pathology's most common findings . . . Of course we are not all ill, but we do all contain some pathology, of which one dead cell is just a trivial example. (Boorse, 1997, 50–51, 85)

Wakefield offers a long, careful analysis of my argument and finds in it a fatal flaw.

> [T]his argument goes wrong due to equivocations between a diseased or disordered individual and a diseased or pathological or disordered part of an individual . . . [A] diseased or pathological part of an individual . . . is compatible with the individual's being completely healthy. . . . The problem for Boorse is that although pathologists [as he claimed] recognize pathology at every physiological level, pathologists . . . do not judge that any pathology at any physiological level constitutes an individual's lack of health or medical disorder. (2014, 654–655)

Later, Wakefield suggests that this distinction (1)—between disease of a part and disease of the organism—can be redescribed as the distinction (2) between (merely) biological and medical pathology:

> Just as Boorse held there was a broad and narrow meaning of "disease," there appear to be broad and narrow meanings of "pathology." The broad meaning refers to "biologically pathological," a concept within biology that covers all part-dysfunction. The narrow meaning refers to "medical pathology" in the sense of medical disorder. (2014, 660)

The two distinctions coincide because he agrees with what he sees as my view that "[t]he indisputable touchstone for entering the medical domain is direct implications for judging the health of an individual" (Wakefield, 2014, 677). However, since he cites not a single biologist or pathologist contrasting "biological" with "medical" pathology,[3] his only evidence for distinction (2) is distinction (1).

Let me first observe that distinction (1), and therefore also (2) because it rests entirely on (1), cannot, despite Wakefield's frequent use of it, help establish his thesis that the HDA beats the BST by including a harm clause. It could do so only if distinctions (1) and (2) coincided with (3) harmless versus harmful dysfunction. But they do not, in virtue of his remarks on homosexuality (Wakefield, 2014). Wakefield defends the coherence of Robert Spitzer's idea that even if homosexuality involves a mental dysfunction, it is still not a mental disorder because it is not harmful. Yet one can scarcely view homosexuality as a dysfunction only of a part, not of the whole organism. Sexual orientation does not resemble Wakefield's alleged BST counterexamples, which feature purely local dysfunctions with no gross effects. How could a part, but not the whole organism, be pathologically sexually attracted to other organisms of the same sex? But then in almost none of Wakefield's examples from physical medicine can distinction (1) support a harm clause. They might support a different criticism of the BST: namely, that it fails to draw distinction (1). But that failing I could correct just by doing so and revising the passages that Wakefield cites accordingly. Only a harmless dysfunction of the whole organism which is not a disorder could argue for adding a harm clause to the BST, so revised. But of Wakefield's 10 alleged counterexamples from somatic medicine, at most two (donated kidney, §IV below; C-III, §IV) fit that category.

Can Wakefield escape this logical problem by abandoning Spitzer and holding that dysfunction of the organism is always harmful to it—that is, that harmful dysfunction is entailed by organism-dysfunction? No, not without drastic change in the HDA. The part-organism distinction is a value-free scientific notion, and so, according to Wakefield, is the concept of biological function. To conjoin two value-free concepts cannot produce a value-laden one. Yet harm, for Wakefield, is an evaluative notion, making his HDA "a hybrid fact/value account of disorder" (2014, 650). Also, to take the line that organism-dysfunction entails harm means that what distinguishes the HDA from the BST is not a harm clause, but an organism clause. So again we see that the diseased part/diseased organism contrast cannot help Wakefield establish his thesis: that the HDA is superior to the BST partly because of its harm clause. Wakefield might reply that organism-dysfunction is merely a necessary condition of harmful dysfunction, but that this is enough for the absence of the former to explain the absence of the latter. At best, however, that seems a puzzlingly indirect strategy to use in arguing for a harm clause.

What, in any case, are the merits of the part-whole distinction itself? Wakefield is quite right to say: "[I]t is as if Boorse assumes that the thesis that part-pathology equals medical disorder [i.e., organism-pathology] is so manifest that it cannot be challenged" (2014, 657).[4] I do assume that disease in an organism is automatically disease of the organism, and so that no organism with a diseased part can

be in perfect health. If you have a diseased pancreas, then you have pancreatic disease.[5] There is no gap between these statements; they are synonymous. In even more detail, statements 1–3 are synonymous and entail 4, which entails 5:

1. There is a disease in your lung.
2. You have a diseased lung.
3. You have a lung disease.
4. You have a disease.
5. You are not completely (or perfectly) healthy.

Logically, I suppose the concept of disease could have worked the way Wakefield says, in which case I would commit a fallacy of composition between 2 and 3. But his part-whole examples do little to support this possibility. True, that an organism has a red part (blood) does not imply that the organism "is red" (Wakefield, 2014, 657). But it does imply that the organism is partly red, and so not totally non-red. Similarly, I assumed against Nordenfelt that an organism with a diseased part is partly diseased, and so not totally or perfectly healthy. Somewhat more helpful to Wakefield is the other example he discusses. True, that an organism has a dead part does not imply that the organism is dead—or even, perhaps, partly dead. However, we do often speak of trees and other plants as partly or mostly dead. Nevertheless, Wakefield's distinction (1) might be thought to be supported by the distinction some writers draw, in the literature on defining death, between the death of an organism and the death of its parts.[6]

But for "disease" itself, not "death," standard medical usage shows no trace of Wakefield's distinctions. On the contrary, disease of a part—even if purely local, asymptomatic, and wholly subclinical[7]—is always disease of the organism. To illustrate the point, let us first consider two disease names: "tinea pedis" and "chronic prostatitis." Tinea pedis or athlete's foot, "the most common dermatophytosis," is a fungal infection of the outermost layer of skin, the stratum corneum, or of the nails (Porter, 2011, 708). It is "usually a chronic, lifelong infection," which flares up in symptoms only in periods when moist conditions favor fungal growth (Epstein, 2001, 169). At such times, one treatise calls it "overt tinea pedis" or "symptomatic athlete's foot" (Freedberg et al., 1999, 2351, 2350). However, "[m]any persons have the disease and are not even aware of it" (Hall, 2000, 200); indeed, "[a]pproximately 10 percent of the total population can be expected to have a dermatophyte foot infection at any time" (Freedberg et al., 1999, 2349). Now all dermatology textbooks that I have seen call the disease "tinea pedis" at all stages, including the chronic subclinical infection. But tinea pedis is of course a disease of the individual, not merely of his part. "Tinea pedis of the foot" is either redundant (because "pedis" means "of the foot") or nonsensical (because a foot has no feet). By definition, only a person, not a foot, can have tinea pedis. There can be tinea in your foot, perhaps, but when there is, you have tinea pedis.

A similar example, representing a broad class, is asymptomatic chronic prostatitis. In the era of prostate-specific antigen (PSA) screening, untold thousands of men were relieved to receive this diagnosis, instead of one of cancer, after a biopsy provoked by high or rising PSA levels. In most of these men, the disease was wholly asymptomatic. Indeed, Wikipedia tells us that "[b]etween 6–19% of men have pus cells in their semen but no symptoms." So, here again, we have a disease most cases of which are purely local, asymptomatic, and apparently harmless.[8] But again the disease name itself shows that it is a disease of the person, not just of his part. "Prostatitis" means inflammation of the prostate, just as "tinea pedis" means tinea of the foot. By definition, only a person, not a prostate, can have prostatitis. A prostate can be inflamed. But when your prostate is inflamed, you have prostatitis. And so it is throughout the enormous range of diseases defined via pathological terms, such as those ending in "-itis." No matter how local and harmless the disease's effects in a specific case may be,[9] the disease is always a disease of the person. All diagnoses are of the person.

III. MEDICAL TERMINOLOGY IN THREE CHRONIC, INITIALLY SUBCLINICAL DISEASES

For deeper insight into standard medical usage, let us examine three major, often fatal, chronic diseases. One reason why medical terminology is confusing is Kendell's observation that disease definitions are of many heterogeneous types.

> Each of these waves of technology has added new diseases, and from each stage some have survived. A few, like senile pruritus and proctalgia fugax, are still individual symptoms. Others, like migraine and most psychiatric diseases, are clinical syndromes—Sydenham's constellation of symptoms. Mitral stenosis and hydronephrosis are based on morbid anatomy, and tumours of all kinds on histopathology. Tuberculosis and syphilis are based on bacteriology and the concept of the etiological agent, porphyria on biochemistry, myasthenia gravis on physiological dysfunction, Down's syndrome on chromosomal architecture, and so on. (1975, 307)

Of my three examples in this section, the first disease—emphysema—is straightforwardly defined via pathology (Kendell's "morbid anatomy"), with little terminological confusion. The second—type-1 diabetes mellitus—is clinically defined. But as in all three examples, the underlying disease process, for which there here seems to be no standard name, runs for years before it is clinically detectable. The third disease—coronary atherosclerosis—is also defined via pathology. But because of its near-universal prevalence (in orthodox medical thought), the diagnoses "coronary artery atherosclerosis" or "coronary heart disease" are commonly restricted to late, clinically manifest cases.

Emphysema

In its section titled "Chronic Obstructive Pulmonary Disease" (COPD), the Robbins pathology textbook states: "Emphysema is defined in terms of the *anatomic nature* of the lesion . . ." (Cotran, Kumar, and Collins, 1999, 707). Specifically, it is "a condition of the lung characterized by *abnormal permanent enlargement of the airspaces distal to the terminal bronchiole, accompanied by destruction of their walls*, and *without obvious fibrosis*" (Cotran, Kumar, and Collins, 1999, 707). The textbook proceeds to subdivide emphysema, so defined, into four categories by "anatomic distribution": centriacinar, panacinar, paraseptal, and irregular. However, it says such classification "can be done only on postmortem specimens" (Cotran, Kumar, and Collins, 1999, 707). It then notes that "only the first two" of these types "cause clinically significant airflow obstruction" (Cotran, Kumar, and Collins, 1999, 707). One of the others, "irregular," may be "the most common form of emphysema"—so common, in fact, that "careful search of most lungs at autopsy shows one or more scars from a healed inflammatory process. In most instances, these foci of irregular emphysema are asymptomatic" (Cotran, Kumar, and Collins, 1999, 709). In any case, "[t]he clinical manifestations of emphysema do not appear until at least one-third of the functioning pulmonary parenchyma is incapacitated" (Cotran, Kumar, and Collins, 1999, 710).

With one exception, this pathology textbook's terminology is quite clear. Unlike its companion disorder in the COPD category, chronic bronchitis, which "is defined clinically," emphysema is defined by pathology (Cotran, Kumar, and Collins, 1999, 711). Any person who has a certain type of lung lesion has the disease, and as a result, it is present in as much as half the population. But most cases are, and will remain, subclinical. A clear distinction is made between emphysema and its "clinical manifestations." Even this book, however, cannot avoid some of the conceptual laxity of medical language, since it defines COPD, the category to which emphysema belongs, as "a group of conditions that share a major symptom—dyspnea—and are accompanied by chronic or recurrent obstruction to airflow within the lung" (Cotran, Kumar, and Collins, 1999, 706). Medical readers are not confused by this statement, even though dyspnea is absent in most cases of emphysema.

More confusing, however, is the Medscape overview of emphysema, which reports a much lower "prevalence."

> The National Health Interview Survey reports the prevalence of emphysema at 18 cases per 1000 persons and chronic bronchitis at 34 cases per 1000 persons. . . . This prevalence is based on the number of adults who have ever been told by any health care provider that they have emphysema or chronic bronchitis. This is felt to be an underestimation because most patients do not present for medical care until the disease is in its later stages. ("Emphysema", July 2015)

In other words, these figures are for the prevalence not of emphysema, but of emphysema sufficiently advanced to be not only symptomatic, but clinically diagnosed. And if the prevalence of emphysema, according to pathologists, is already known to be nowhere near 1.8%, but closer to 50%, this is strong evidence that Medscape and its source are using "emphysema" to mean "*symptomatic* emphysema." A

roughly 25-fold discrepancy is evidence, not of uncertainty, but of exactly the kind of semantic ambiguity between pathologists' and clinicians' usage that I suggest is common in medicine.

Type-1 Diabetes Mellitus

Diabetes mellitus, as its name ("honey-sweet siphon") suggests, seems to be clinically defined by symptoms and clinical signs. *Rubin's Pathology* states:

> The current criteria for the diagnosis of diabetes mellitus are based on determining the abnormal glucose threshold levels that are most closely associated with the chronic complications of this disorder. (Rubin and Gorstein, 2004, 1174)

Specifically, a recent WHO report states cutpoints for diabetes mellitus of 7.0 mmol/L of fasting glucose or 11.1 for 2-h glucose. Lower thresholds define various kinds of "intermediate hyperglycemia," sometimes called "prediabetes" (World Health Organization, 2006, 33, 36). Since these clinical variables are continuous, it is not entirely clear whether WHO intends to define the disease "diabetes mellitus" or merely offer conventional diagnostic criteria for it. Fortunately, this obscurity does not affect my argument in this paper.

However defined,

> Diabetes mellitus represents a heterogeneous group of disorders that have hyperglycemia as a common feature. . . . [T]he most common and important forms of diabetes mellitus arise from primary disorders of the islet cell-insulin signaling system. (Cotran, Kumar, and Collins, 1999, 913)

Of such disorders there are two main types. Type-1 diabetes (also called "insulin-dependent" or "juvenile-onset") is usually caused by an autoimmune attack on the insulin-secreting β cells of the pancreatic islets of Langerhans. Its etiology is thought to combine genetic susceptibility with an environmental trigger. On its pathogenesis, the Robbins text writes:

> Although the clinical onset of type 1 diabetes is abrupt, this disease in fact results from a chronic autoimmune attack of β cells that usually exists for many years before the disease becomes evident. The classic manifestations of the disease (hyperglycemia and ketosis) occur late in its course, after more than 90% of the β cells have been destroyed. (Cotran, Kumar, and Collins, 1999, 916)

Note, however, the conceptual tension in this quotation. Officially, "diabetes mellitus" is, as we saw, a clinical entity with many types of cause. If so, "type-1 diabetes mellitus" must be a type of clinical entity: here, a clinical entity with one particular pathogenesis. Although we can see the writers trying to conform to this logic, they are handicapped by their lack of a name for the process of autoimmune β-cell destruction, as opposed to its eventual clinical effects. Hence their reference to many years in which "the disease" is not "evident." What disease? If diabetes mellitus is defined in terms of hyperglycemia, hyperglycemia cannot occur only "late in its course." What we need is a term—say, "X"—for the autoimmune cell destruction itself.[10] If we substitute "X" for the second two occurrences of "disease," all is clear. Then type-1 diabetes mellitus is just a clinical phase of X: X with sufficiently dramatic signs or symptoms. But X itself is still a disease at all stages, as the book says. And "X" might well not appear in ICD if there is no occasion to discover and code it in the years before abnormal glucose-test results appear.[11]

Coronary Atherosclerosis

Rubin's Pathology describes the disease of atherosclerosis and its development as follows.

> Atherosclerosis is a disease of large and medium-sized elastic and muscular arteries that results in the progressive accumulation within the intima of inflammatory cells, smooth muscle cells, lipid, and connective tissue. The classical atherosclerotic lesion is best described as a fibroinflammatory lipid plaque (*atheroma*). (Rubin and Gorstein, 2004, 483)

> The sequence of events in the development of atherosclerosis . . . may begin as early as the fetal stage, with the formation of intimal cell masses, or perhaps shortly after birth, when fatty streaks begin to evolve. However, the characteristic lesion, which is not initially clinically significant, requires as long as 20 to 30 years to form. (Rubin and Gorstein, 2004, 485)

This text then describes three stages of the disease, the third being "clinical" and the first two being described as "subclinical" (Rubin and Gorstein, 2004, 486).

All this holds for coronary atherosclerosis, in particular. According to Medscape, "The earliest pathologic lesion of atherosclerosis is the fatty streak, which is observed in the aorta and coronary arteries of most individuals by age 20 years."[12] In a strict sense, then, most people—perhaps nearly all adults[13]—have the disease coronary atherosclerosis. Yet Medscape also tells us that "Approximately 14 million Americans have CAD [coronary artery disease]," and CAA (coronary artery atherosclerosis) is the "principal cause" of CAD.[14] What is going on here? Clearly, for prevalence figures, a terminological switch is made to *clinical* CAA. Obviously, far more than 14 million Americans have CAA on the pathologic level. The 14 million are those who have reached what the Rubin text calls the third, or clinical phase, and do not merely have the disease, but also have been diagnosed with it.[15] And, of course, clinically diagnosed CAA must also be meant when CAA (or CHD) is made a "risk factor" in official guidelines for treating conditions like hypertension, hypercholesterolemia, and atrial fibrillation. It would have no information value to call a disease a risk factor if, like CAA in the pathological sense, it is already known to afflict nearly the whole adult population.[16]

Medicine offers innumerable such examples of chronic, local, subclinical disease processes, pathologically defined, which progress over many years before signs and symptoms appear. In some cases, the common disease name covers all phases of the process (emphysema, CAA); in others, the common disease name is reserved for the clinical stage (type-1 diabetes mellitus). Even when the name covers all stages, it is also sometimes used in a narrower clinical sense (emphysema, CAA). But at all stages, the process is called a disease.

Finally, it is surely a disease of the organism, not merely of its part. When 30% of lung parenchyma is already lost to emphysema, who would say that it is still only a disease of the lung, not a lung disease of the person? The same goes for the time, shortly before the clinical onset of type-1 diabetes, when 85% of β cells are already gone. To take such a view would amount simply to denying that human beings can have subclinical disease—a concept fundamental to scientific medicine. Unfortunately, as we shall see in §IV, that is exactly what Wakefield does. Nor is it plausible to say that patients about to experience their first dyspnea or hyperglycemia are still in perfect health. Notoriously, the first clinical manifestation of CAA is often a fatal heart attack, when an advanced atheroma ruptures. But no one in medicine would say that someone can be in perfect health at one instant, then spontaneously drop dead the next. Such a person was, of course, apparently in perfect health; but in reality, he suffered from advanced heart disease. That is the universal medical description of such a condition.

But if clinical onset does not separate purely biological disease of a part from genuinely medical disease of the organism, then nothing does. There is no such boundary: "medical disease" goes all the way down. Whatever name we give his condition, the future type-1 diabetic has a disease from the moment his first T-lymphocyte attacks his first β cell. That is the position of the BST, and the only one that fits medical usage.

IV. WAKEFIELD'S PURPORTED COUNTEREXAMPLES TO THE BST

What are we to say of Wakefield's fascinating, often lavishly researched collection of counterexamples to the BST—that is, of alleged harmless part-dysfunctions not classified as disorders? The only generalization I see is that no medical source Wakefield quotes uses his distinction (1) or (2) to describe any of these cases. None, that is, says the condition is biological but not medical pathology, nor a disease, disorder, dysfunction, or pathological condition of a part but not of the organism. Rather, Wakefield translates his sources' words into his own vocabulary. Besides gene mutations, which merit a paper of their own, the examples fall into two groups.

Noninfectious Examples

Missing kidney after organ donation

ICD-10 classifies "acquired absence of kidney" as Z90.5, right after its Z89 section on acquired absence of limbs. But I give little weight to any medical classification's treatment of surgically absent organs. Medical writers often seem to assume that the result of justified medical treatment cannot be pathological, which is merely silly. In reality, all surgery produces pathology, if only a tiny scar. Most surgery aims to replace greater pathology with lesser pathology.

In any event, Wakefield cites three studies finding that kidney donation has no effect on life expectancy, reproductive success, or even "overall kidney function" (2014, 661). But no such effects—even gross organ dysfunction—are necessary conditions for disease status, for the reasons I stated in the paragraph that Wakefield quotes. The kidney is yet another organ with huge built-in reserve capacity. In the early stages of chronic kidney disease, measurable renal function can remain normal until somewhere near 50% of the nephrons are destroyed (Harrison and Thorn, 1977, 1421). In medicine, such a condition is called "compensated disease."[17] So, if "overall kidney function" is unimpaired in early cases of undoubted disease of one kidney, then similarly unimpaired function cannot show that the complete absence of the same kidney is not a medical disorder. I have said before that it is, and I see no reason to change my view (Boorse, 1997, 49). And it is certainly a disorder "of the individual," not of the missing organ, since that organ now resides happily in someone else.[18]

Incompetent sperm

As a cell type, spermatozoa are unique in several ways. First, they are not attached to the body, have a very short life, and, as the suffix "-zoa" indicates, are more like new half-organisms than like body cells. For that reason they show tremendous genetic variation, accounting for half the variation between siblings. Second, unlike cells in body organs, only an infinitesimal quantity of them ever perform any biological function at all. Even when sex leads to conception, as it usually does not even in a state of nature, only one or a few of the roughly 300 million sperm in a healthy man's ejaculate can win the race. So, unlike in other tissues, it is completely impossible for all these cells to perform their (only) function, or even for all of them to be ready to perform it. Three hundred million swimmers cannot all be ready to win a race.

Presumably this brutal competition, in which only the very fittest sperm survive,[19] was itself designed by natural selection to maximize reproductive success. At any rate, these unique features explain why dead or incompetent sperm will be observed in almost any human semen sample. And they make it more reasonable for us to regard the ejaculate, not the individual spermatozoon, as the relevant functional unit. Accordingly, we find the *Oxford Handbook of Reproductive Medicine and Family Planning* only requiring a "normal" semen sample to have <25% dead sperm, <50% sperm with defective motility, and <35%, <20%, and <20% sperm with morphological defects of the head, midpiece, and tail, respectively (McVeigh, Hamburg, and Guillebood, 2008, 168). The alternative to this view, it seems, is not only to regard every male mammal as having a spermiogenetic disease, but to view a kind of pathology as inherent in the mammalian design. The BST cannot accept such a proposition. Readers will recall that my statement that "one dead cell" is pathological only relates to tissues that, unlike sperm, do not function via "constant death and regeneration" (Boorse, 1997, 50).

Situs inversus totalis

Wakefield quotes old and new medical sources describing situs inversus totalis (SIT), the complete (and uncomplicated) left-right reversal of thoracic and abdominal organs. His claim is that both the eminent 18th century pathologist Matthew Baillie and contemporary writers view SIT as due to a dysfunction which, because harmless, is not a disease or disorder. However, he puts one of the key words in all his sources' mouths. Not one of his sources uses the term "dysfunction," or anything equivalent, for SIT.

Baillie calls SIT a "lusus naturae," a "monstrosity," a "great deviation in nature," and Wakefield's modern writers call it "abnormal," "incorrect," and a "defect," "anomaly," and "malformation" which is the "opposite" or "reversal of normal" (Wakefield, 2014, 669–670). Here the term "normal" itself could be read as statistical normality. The rest, however, suggest that the writers see SIT as some form of pathology—necessarily pathology of the organism, not of the individual organs. If that is their view,

then there is nothing new here for me to dispute. I have conceded from the first that some medical sources classify some purely structural abnormalities lacking dysfunction, such as macacus ear and unusual hymens, as pathological (Boorse, 1997, 565–566). In my view, such classification is mistaken: it confuses statistical normality with true medical normality. Without dysfunction, these conditions are abnormal only in a statistical sense, not in the genuinely medical sense of being pathological.

As to dysfunction, Baillie's only relevant quotation flatly denies it: "it does not appear, that the functions can be affected" (Wakefield, 2014, 670). Nevertheless, Wakefield heroically attributes to Baillie, as well as to modern writers, the idea of dysfunction in the orienting mechanism, which is now thought to be the rotation of certain cilia:

> In sum, Baillie believed that the observed systematic positional transformation of the organs is clearly a dysfunction, yet one from which there is no harm . . . Baillie, like more recent accounts, assumes that standard orientation is biologically designed and infers the existence of a part-dysfunction in the responsible mechanisms. However, he judges the dysfunction to be a nondisorder because there is no subsequent harm to the organism. (2014, 670, 672)

Baillie aside, if SIT currently has no ill effect on individual survival or reproduction (S&R), then the cilia's deviant behavior is not a dysfunction by my analysis of biological function (Boorse, 1976). The cilia in question may have a statistically normal effect, in our species, of producing the typical orientation. But that effect is not, for me, a function (in the sense relevant to health) if it does not promote S&R. If SIT never reduced S&R in the past either, then the cilia's typical action is not the product of natural selection and likewise has no function on Wakefield's (1999) own selectionist analysis of function.[20] If it had such an effect in the past and was selected for it over the SIT version, then on Wakefield's analysis the cilia's typical rotation does have a function today, even though it is of no use to the organism. In that case, SIT is one more example of the implausibility of selectionist accounts of biological function.

Apolipoprotein C-III

C-III, as Wakefield describes it, is essential to triglyceride production. Some people are heterozygous for a mutant knockout allele of the C-III gene, which lowers their triglyceride level and so their risk of cardiovascular disease. Thus,

> In a modern environment . . . high but normal-variant levels of triglycerides [are] harmful, so . . . [the mutation] turns out to be beneficial without any apparent cost. This, then, is a real example of a harmless dysfunction . . . (Wakefield, 2021b, 519)

One might think that this example can be dispelled in either of two ways. If Wakefield means that the mutation is beneficial in some but harmful in other modern species-typical environments, then he assumes false environmental relativity of disease. Just as there is no such concept in medicine as "X is a disease for person P," as Wakefield (2021c, 557) correctly states, there is also no such concept as "X is a disease in environment E." (For detailed argument, see Boorse, 2021, 33–35.) In that case, the mutation is pathology beneficial in certain environments, just as the regular gene is a normal feature harmful in certain environments (like white skin in the African sun, or our lack of gills underwater). Alternatively, Wakefield might mean that our whole species has now changed, so that the C-III gene is now harmful in all environments. In that case, on an S&R view of function, it has ceased to have any function, like the eyes of blind cave-dwelling fish, and so its mutation is not a dysfunction. The fact that Wakefield believes the harmful C-III gene still to have a function would be yet another example of why selectionist theories of function are implausible.

Unfortunately, since a double dose of the mutation is harmful in all environments, this example, like the sickle gene, suffers the added complication of heterozygote superiority. I have discussed sickle trait elsewhere, concluding that although both the BST and medicine seem to classify it as pathological, perhaps in heterosis the disease concept is too vague to give a clear answer (Boorse, 1997). Anyway, however one analyzes the sickle gene, a similar analysis would apply to the C-III knockout gene too.

Microbial-Infection Examples

Asymptomatic carriers (Typhoid Mary)

Wakefield says that Mary Mallon, "the first widely recognized symptomless carrier of typhoid fever," had a clear part-dysfunction because "live typhoid bacteria were actively replicating within her" (2014, 663). He says that both in her era and today,

> [m]edical and lay descriptions simultaneously recognize the internal bacteriological pathology of her infection—indeed, there could not be a clearer case of internal dysfunction than Mary's, with bacteria utilizing her gall bladder as a spawning ground—and yet judge her to be healthy and free from disease . . . (Wakefield, 2014, 663)

He quotes four sources, plus Mary herself, to establish that she was "healthy and free from disease" (Wakefield, 2014, 663). Since carrier status for communicable disease is, to this day, in "nondisorder" category Z of ICD-10, Wakefield concludes that "infection and complete health are not incompatible when the infection causes no symptomatic harm" (Wakefield, 2014, 664).

We have already seen with tinea pedis, and will see again below, that harmless atypical infections, not only asymptomatic but entirely subclinical, are still medical diseases of the organism, and classified as such in ICD-10. In Wakefield's quotations, no medical source actually says that Mary is completely healthy and free of disease. How could she be, when her gallstones,[21] of which her doctors were presumably aware, are themselves a pathological condition (cholelithiasis, K80)?[22] Two lay sources—*The New York Times* and Mary—call her healthy. But they may mean no more than what the quoted physicians actually say: that Mary does not have, and has never had, the specific disease typhoid fever. That does not show that carrier status is not a (different) disease, any more than the fact that someone with subclinical autoimmune β-cell destruction does not have type-1 DM means that the β-cell destruction is not itself a disease. Mary's public-health nemesis George Soper, a sanitary engineer, does say that her condition is "not a disease," but he was not a physician. Unlike Wakefield, I place no weight on lay usage, and little weight even on medical judgments in the early years of a new science like bacteriology, when conceptual clarity is in short supply.

Wakefield also leaves out two seemingly relevant facts about Mary's case. First, Soper's own article reports that Mary's death certificate lists her cause of death as bronchopneumonia, chronic nephritis, and chronic myocarditis, to which 24 years as a typhoid carrier was "contributory" (1939, 712). So, apparently, Mary's carrier status was not so harmless after all. Second, Mary managed in 1909 to litigate her confinement, provoking a judicial decision unfavorable to Wakefield's view. §1170 of the Greater New York Charter gave the Board of Health authority to confine "any person *sick with* any contagious, pestilential or infectious disease" (italics added). Before a judge of the NY Supreme Court, Mary's lawyer argued that, being symptom-free, she was healthy, not sick, and so could not be confined under New York law. But Judge Erlanger apparently believed that the state's evidence of typhoid bacilli in Mary's stool samples sufficed to make her sick for legal purposes,[23] so he remanded Mary to the custody of the Board of Health. While I would certainly not call Mary "sick," this court judgment, like that of the US Supreme Court on HIV in *Bragdon v. Abbott* (§IV below), offers some evidence that the condition was viewed as a disease.

As for contemporary views, contrary to Wakefield, section Z of ICD-10 is not limited to nondisorders. It includes Z89, "acquired absence of limb." It would be strange indeed to describe a person with no arms or legs (Z89.8) as in perfect health; certainly, such a person is not medically normal. Nor, for that matter, does a Z listing exclude even infectious disease. Section Z20 is for "Contact with and exposure to communicable diseases." A person who is coded, say, Z20.3 is known to have exposure to rabies and not known to have the disease—but also not known not to have it. If rabies symptoms appear, his code changes to A82.9. Somewhat analogously, typhoid carriers might be reclassified when the nature and site of their infection (gall bladder, liver, intestine) become known. Until then, carrier status (Z22) is important information to have in a person's chart. But it is, in theory, consistent with the thesis that all carriers have specific codable pathology of some sort.

Is that thesis true? Wakefield says "there could not be a clearer case of internal dysfunction" than Mary's typhoid carriage (2014, 663), but I am not so sure. Surely the mere fact that bacteria are multiplying in her gall bladder does not show dysfunction. After all, the "normal flora" grow in the gut

without dysfunction, too (see below, §III), and they are no more and no less inside the organism than Mary's *S. typhi*. To a physiologist, none of these bacteria are inside the organism until they cross a cell membrane. It is not clear to me why *S. typhi* growing within a biofilm on a gallstone, yet damaging no body cells, must be a dysfunction, even one of the immune system. Such dysfunction is more plausible in the other two mechanisms of carriage named by Medscape: growth in or on the gall-bladder epithelium. Yet a fourth recently discovered mechanism is *S. typhi* growth within macrophages, whose normal lytic function the bacilli somehow block. That looks like a clear part-dysfunction, conceptually somewhat like a Ghon lesion (§IV). But a further complication is that, as one biologist suggests, carriage might be an evolutionary adaptation, to save a host the expense of the full-blown systemic immune response seen in typhoid fever itself.

On the whole, I am inclined to think that whether carrier status involves dysfunction may vary with its exact mechanism. But surely Wakefield is right that "injury or destruction of" cells other than immune-system cells, by multiplication of pathogens within them, must involve dysfunction, unless there is a countervailing benefit (2014, 665).

Latent stages of infectious disease

Latent tuberculosis

Our first example here is latent tuberculosis. Both Wakefield (2013) and Rogers and Walker (2017) suggest that the BST mishandles TB because the latent stage of infection with *Mycobacterium tuberculosis* is not considered in medicine to be a disease. Wakefield writes: '"[T]uberculosis is an infectious disease' . . . is true, yet few people infected with tuberculosis develop disease because most people's immune responses contain the infection . . ." (2013, 2) But it is certainly not standard medical usage to call only active, not latent, TB pathological. The hallmark of latent TB is the Ghon lesion, which is, of course, a lesion, hence pathological by definition. It is coded by ICD-10 in a section with "disease" in its title ("Certain infectious and parasitic diseases," WHO, 1994).[24] By classic usage, it is no more controversial that latent TB is an intermediate stage of TB than that latent syphilis is an intermediate stage of syphilis.

There are two coherent terminological options. One, typical of older discussions, calls the latent infection "latent tuberculosis." In that case, it is a type or phase of tuberculosis, contrasting with "active tuberculosis." The second option is to reserve "tuberculosis" for the active phase, somewhat as "diabetes mellitus" is reserved for a clinical entity. In that case, the latent infection, often called LTBI (latent tuberculosis infection) is a different, precursor disease state. In current textbooks, one sees a mildly confusing mixture of these two options, the latent TB/active TB terminology and the LTBI/TB terminology. But such confusion no more casts doubt on whether LTBI is a disease state than similar terminological confusion about type-1 diabetes mellitus casts doubt on whether autoimmune β-cell destruction is a disease state. Whatever it is called, latent tuberculosis is a pathological condition.

Asymptomatic HIV infection

Wakefield (2014, 667) notes that ICD-10 does not classify mere HIV infection in the infectious-diseases section called "HIV disease," but instead relegates it to a Z code. As we have already seen, Z-coded conditions can be disorders (missing limbs). However, I agree that if HIV infection is already a type of "HIV disease," it should be in section B24, "Unspecified HIV disease." Perhaps the WHO writers thought it would be less confusing to reserve §§B20–B24 for clinically evident effects of HIV infection, besides the blood test itself. Nevertheless, we see conceptual sloppiness here, since asymptomatic HIV infection is just one phase of HIV disease.

It is of at least minor interest that 6 years after ICD-10 was published, the U.S. Supreme Court held 5-4—with no dissent on this issue—that HIV infection is a "physiological disorder" at all stages. Since its detailed analysis is too long to quote here, I instead quote my own summary of it:

> In *Bragdon v. Abbott* [524 U.S. 624 (1998)], a five-person majority held that HIV infection is always an impairment, even in its initial and its later "asymptomatic" phases. But the majority's reason is precisely that HIV infection at any stage is a medical disorder. It assumes, in the initial stage, an "immediate" "assault on the immune system" and "a sudden and serious decline in the number of white blood cells." . . . The Court says the term "asymptomatic phase" is "a misnomer," since "clinical

> features persist throughout, including lymphadenopathy, dermatological disorders, oral lesions, and bacterial infections." All of these are pathological conditions that can be coded as such in ICD-10. "In light of these facts," the court concludes, "*HIV infection must be regarded as a physiological disorder* with a constant and detrimental effect on the infected person's hemic and lymphatic systems *from the moment of infection*" (Boorse, 2010, 74, italics added).[25]

Insofar as the Court's factual foundation differs from ICD-10's, its judgment may be irrelevant to Wakefield's argument. But the opinion does at least include a ringing declaration that a condition that seemed "asymptomatic" to WHO can still be a medical disorder.

Commensal bacteria and viruses

In the terminology of one of Wakefield and Conrad's (2020) sources (Roossinck, 2011, 99–100), two organisms living in close association—symbiosis in the broadest sense—may have a relationship that is antagonistic, mutualistic, or commensal. A commensal organism is one that benefits by living with another one that is indifferent to it, being neither benefited nor harmed (Tannock, 1999, 1). Note that strictly, by the definition just given—despite loose common usage including some of Wakefield and Conrad's sources—an animal's normal microbial flora are not commensals, since "each partner influences the other markedly" (1).

Wakefield and Conrad cite examples of both bacteria and viruses to argue that a "naturalistic" account of disease like the BST violates medical usage, since such infections are dysfunctions that are not pathological. Their chosen bacterium is *Streptococcus pneumoniae*. Although, they say, every infection with it is a "dysfunction," most are not called pathological because "the vast majority of infections occur harmlessly in the nose and sinuses, and the bacterium only becomes problematic under special circumstances" (Wakefield and Conrad, 2020, 357). As for viruses, besides HIV, Wakefield's examples are the Epstein-Barr virus, which he and Conrad say "exists in roughly 95% of the world's adult population," and poliovirus (2020, 357–358). Both, they say, cause disease in only "a small minority of cases" of infection (Wakefield and Conrad, 2020, 358). Yet, they argue, viral infection entails dysfunction:

> [E]very cell virus replicates by using the genetic machinery that is biologically designed for other purposes and so causes a dysfunction. Consequently, the naturalist-dysfunction account [such as the BST] would imply that every viral infection—at least every infection that is active as opposed to latent—would be a disorder, whether harmless or not. (Wakefield and Conrad, 2020, 358)

So the discovery of commensal viruses is, our authors think, a "natural conceptual experiment" that tests "[t]he naturalist prediction that all viral infections will be considered diseases" (Wakefield and Conrad, 2020, 359, 358). The fact that scientists, again, do not call such harmless infections diseases "decisively falsifies the naturalist hypothesis" (Wakefield and Conrad, 2020, 359).

This argument fails, however, for at least three distinct reasons, some of them evident from Wakefield and Conrad's own sources. First, on the BST, nothing species-typical is a disease (Boorse, 1977). Only statistically species-subnormal function is pathological; the typical effects of normal flora are as normal as can be. This is especially obvious for bacteria like *E. coli*, present in virtually all human colons from shortly after birth, since they are not even inside the organism, only on its inner surface.[26] But the typicality point applies equally to a virus like Epstein-Barr inside human cells. If it is present in 95% of human beings, then its typical effects are normal, according to both medicine and the BST. The fact that, as with most viruses, its reproduction in the lytic or "active" phase kills host cells does not disturb this point (Wakefield and Conrad, 2020, 358). Almost all human cell kinds have a typically limited lifespan, and in some cases their death is essential to normal function. For example, the outermost layer of skin consists of corneocytes, which are essentially dead cells. Thus, if a normal-flora virus reduces the typical lifetime of a particular kind of human cell, the BST calls the resulting cell death normal, not pathological. That becomes even clearer when the viral infection has benefits, which brings us to the next point.

Second, typicality aside, there is no reason why even "active" viral infection must be dysfunctional. Wakefield and Conrad assume that any use of "genetic machinery that is biologically designed for other purposes" must be a dysfunction. But that is not so. Even if a part has evolutionarily designed

functions, other uses of that part are not necessarily dysfunctional; recall Wright's example of noses holding eyeglasses. Insofar as any viral infection benefits the host, to support virus multiplication may be a part of that cell-type's normal function. At least the normal flora are almost always somewhat beneficial to the host. One infectious-disease treatise says: "The normal, commensal flora constitute a critical ecosystem that plays an important role in protecting the host from microbial invasion by 'pathogenic' organisms." It then lists six such "protective mechanisms" (Mandell et al., 2000, 31). Wakefield and Conrad's sources agree; the two Roossinck articles are explicitly about "mutualistic" viruses. She describes such viruses as "critical symbiotic partners in the health of their hosts" (Roossinck, 2015, 6532), and writes:

> Although viruses are most often studied as pathogens, many are beneficial to their hosts, providing essential functions in some cases and conditionally beneficial functions in others . . . These include viruses that have a long association with the host, so that the relationship has become essential for the survival of the host; viruses that attenuate diseases caused by other viruses or other pathogens; viruses that are useful to their hosts because they kill competitors; viruses that help their hosts adapt to extreme environmental changes; and viruses that are involved in complex multispecies interactions.[27] (Roossinck, 2011, 99, 100)

In short, many of the relations loosely called commensal, by Wakefield and Conrad and their sources, are actually mutualistic. In that case, regardless of prevalence, the BST again has no need to recognize dysfunction, if the virus's net effects are beneficial, or even net-neutral. At most, it declares (atypical) antagonistic symbiosis pathological, not mutualistic or commensal.

Third, as we saw earlier with Wakefield's discussion of Typhoid Mary, most of his sources do not say what he and Conrad say they do. It is not true that these sources "classify" commensal viruses as "nondisordered" (Wakefield and Conrad, 2020, 359). For one thing, none of the sources uses the term "disorder" to refer to infections at all. Nor do most of these writers deny that infection with bacteria or viruses besides normal flora is disease, or pathological. Rather, they usually contrast it with "overt" or "symptomatic" or "acute" disease (Virgin, Wherry and Ahmed, 2009, 30; Virgin, 2014, 142, 144; Vu and Kaiser, 2017, 688). Obviously, if all diseases, or even all infectious diseases, were overt and symptomatic, these qualifiers would be unnecessary. And just as with Mary and typhoid fever, we sometimes see the term "healthy" used to mean the absence of overt disease, allowing "healthy" individuals to have a "chronic carrier state" for pathogenic bacteria or viruses (Virgin, 2014, 144). Virgin, Wherry, and Ahmed (2009) offer a long list of such viruses. On the whole, then, regarding microbes that are not normal flora, Wakefield and Conrad's sources well fit our earlier view of HIV and typhoid: that all such infections involving "tissue damage" without benefit are pathological conditions, but not necessarily called by the same name as the corresponding clinical entity (e.g., typhoid fever) (Virgin, Wherry, and Ahmed, 2009, 31).[28] Thus, for all these three reasons, there is no clear evidence that Wakefield and Conrad's sources contradict the BST by citing dysfunctions that are not pathological.

We should also mention, however, another possibility: that some, even many, infections are just borderline cases of trivial pathology. Not only are the interactions among host cells, bacteria, and viruses amazingly complex (Roossinck, 2011; Virgin, 2014), but in many ways, we can also expect vagueness in whether to call them normal or pathological. It may be unclear whether a relationship is antagonistic, mutualistic, or commensal, especially since relationships vary over time (Roossinck, 2011, 100). Even as to cell damage and death, it is always somewhat vague how much is needed to be pathological. I said against Nordenfelt that "one dead cell" is not necessarily pathological in "tissues whose normal function entails constant death and regeneration" (Boorse, 1997, 50). But mucosa, where many of the microbes we are discussing live, is a prime example of tissue continually shed and rebuilt. It can even be unclear when a virus is part of the host itself. A substantial part of our genome resulted from a process called endogenization, where, over evolutionary time, viruses permanently merge into their host.[29] It is generally agreed that all nonmathematical concepts, at least, have borderline cases, including biological ones. (Are viruses organisms?) And Wakefield and Conrad (2020) concede that vagueness per se is no objection to a concept of disorder, or to an analysis thereof. In my view, for infection as for other phenomena, the BST either matches the vagueness of the medical concept or helpfully reduces it.

In any event, what alternative view of "mild infection" do Wakefield and Conrad offer (2020, 352)? Remarkably, they just deny the existence of subclinical disease! This view, only hinted at in Wakefield's (2014) critique of the BST, is explicit in 2020. "Here, too, among viral infections, disease is distinguished from nondisease by the presence or absence of harmful symptoms" (Wakefield and Conrad, 2020, 358).[30] In reality, as we saw in §§II and III, contemporary medicine views disease as often or even usually subclinical, both in general and in infections (e.g., tinea pedis). To cite one of Wakefield's favorite sources, the CDC, its introduction to clinical epidemiology divides the "natural history of disease" into the following stages: "susceptibility," "subclinical disease," "clinical disease," and "recovery, disability, or death."

> After the disease process has been triggered, pathological changes then occur without the individual being aware of them. This stage of *subclinical disease*, extending from the time of exposure to onset of disease symptoms, is usually called the **incubation period** for infectious diseases, and the **latency period** for chronic diseases. During this stage, disease is said to be asymptomatic (no symptoms) or inapparent. This period may be as brief as seconds for hypersensitivity and toxic reactions to as long as decades for certain chronic diseases.
>
> The onset of symptoms marks the transition from *subclinical* to clinical disease. Most diagnoses are made during the stage of clinical disease. In some people, however, the disease process may never progress to clinically apparent illness. In others, the disease process may result in illness that ranges from mild to severe or fatal. This range is called the **spectrum of disease**. (Center for Disease Control, 2021, 1–59, 1–60, italics added)

The existence of subclinical disease is not controversial in ordinary medicine; it is accepted even by leading critics of "overdiagnosis."[31] It either is, or is inseparable from, the most basic concept of scientific medicine, having been so for at least the 166 years since Virchow's cellular pathology. One can hardly imagine a more drastic departure from medical thought than to eliminate it. In this respect, the BST fits medicine's disease concept perfectly, while the HDA, in denying subclinical disease, stands worlds apart.

V. FIVE HARMLESS SKIN DISORDERS

Although the existence of subclinical disease amply proves my thesis, it may help to add some examples from the specialty of dermatology, where nearly all diseases are clinical. All five are common medical disorders that are harmless in any natural sense of the term and so-called by physicians in speaking to laymen. By Wakefield's methodology, that should settle the question of harm, since disorder, and therefore its harm component, is supposed to be a concept shared by physicians and laypeople alike (2014, 652). All five are classified by ICD-10 (World Health Organization, 1994), under the codes cited below, in chapters with "Diseases" in their titles: B is under "Certain Infectious and Parasitic Diseases," I is "Diseases of the Circulatory System," and L is "Diseases of the Skin and Subcutaneous Tissue." (All these classifications are unchanged in ICD-11.)

Tinea Versicolor (Pityriasis Versicolor) (B36.0)

Tinea versicolor is "a moderately common skin eruption with characteristics of tannish-colored, irregularly shaped scaly patches causing no discomfort that are usually located on the upper chest and back" (Hall, 2000, 138). Like tinea pedis, it is a fungal infection of the stratum corneum. Unlike tinea pedis, it does not cause significant itching, and therefore no injuries that can be complicated by superinfection. Also unlike tinea pedis, the causative yeast, *Malassezia furfur*, is "considered part of the normal flora," here acting as an "opportunistic" pathogen (Freedberg et al., 1999, 2368). Many people with the disease are unaware of it. For those who are aware, "[t]he presenting complaint is usually a cosmetic one as lesions often fail to tan . . ." (Freedberg et al., 1999, 2368) or, in dark-skinned people, are visible as light spots.

As with other diseases in this section, physicians writing for other physicians tend to call tinea versicolor a "benign" condition. But a doctor writing for laymen may call it "harmless." Thus Epstein says, in the section of his book containing handouts for doctors to give patients: "Tinea versicolor is a *harmless* skin disorder caused by a germ living on normal skin" (2001, P-125; I italicize "harmless" in all quotations).

Seborrheic Keratoses (L82)

According to the Fitzpatrick dermatology treatise, "Seborrheic keratoses are benign skin tumors. They are exceedingly common and most people will develop at least one such tumor in their lifetime, with many developing hundreds of these lesions" (Freedberg et al., 1999, 873). Commonly known as "senile warts," they "are not premalignant and need no treatment unless they are irritated, itchy, or cosmetically bothersome" (Porter, 2011, 746). Since many such lesions have none of those three properties, it is not surprising that Epstein calls them "*harmless*, common skin growths that first appear during adult life" (2001, P-97) and *The Encyclopedia of Skin and Skin Disorders* calls them "completely *harmless* but unsightly" (Turkington and Dover, 2007, 198).

Warts (B07)

The same encyclopedia describes common warts as

> *[h]armless*, contagious growths on the skin or mucous membranes caused by any of more than 50 varieties of papillomavirus . . . About half of all warts disappear on their own between six months to a year after they appear. In many cases they can be left untreated to spontaneously resolve. (Turkington and Dover, 2007, 395–396)

The Fitzpatrick book does not disagree, though its term, as befits a medical-specialty treatise, is "benign":

> Warts, or verrucae, are benign proliferations of the skin and mucosa that result from infection with *papillomaviruses* (PV). These viruses do not produce acute signs or symptoms but induce slow-growing lesions that can remain subclinical for long periods of time. A subset of the human PVs has been associated with the development of epithelial malignancies. (Freedberg et al., 1999, 2484)

An example of the latter fact is that genital warts may presage cervical cancer (Epstein, 2001, 174). Epstein recommends that doctors tell their patients that warts are "*harmless* skin growths" (P-127).

Spider Angiomas (Nevus Araneus, I78.1)

Medscape describes spider angiomas as "asymptomatic benign lesions" that "are common in otherwise healthy children and are present in 10–15% of healthy adults and young children." Notice the term "otherwise healthy," confirming the BST's view that a child with a skin disorder, or any disorder, is not, of course, completely healthy. The Merck manual notes: "The lesions are asymptomatic and usually resolve spontaneously postpartum or after oral contraceptives are stopped" (Porter, 2011, 748).

Cherry Hemangiomas (I78.1)[32]

Also known as "cherry-red" or "senile" angiomas or as Campbell de Morgan spots, "[t]hese *harmless*, dilated capillaries appear as tiny, bright red-to-violet colored bumps," according to the *Gale Encyclopedia of Medicine* (Fundukian, 2011, 646). The *Color Atlas and Synopsis of Clinical Dermatology* says:

> Cherry angiomas are exceedingly common, bright-red, domed vascular lesions, occurring on the trunk, becoming more numerous with advancing age, of no consequence other than their cosmetic appearance. (Fitzpatrick et al., 1992, 164)

The Encyclopedia of Skin and Skin Disorders calls them "*harmless*" (Turkington and Dover, 2007, 75), as does Wikipedia.

Our five harmless skin diseases seem to spell final ruin for the HDA's harm clause. There is no harm in them by any standard consistent with Wakefield's views. At most, there is only cosmetic harm significant to some, but not most, individuals. But that much also holds for homosexuality, which, as I argue in another paper, harms some people enormously more than a tiny red dot on the skin. And Wakefield's two distinctions are no help with these examples. It is no more plausible to call these skin conditions mere diseases of parts than to say the same about our subclinical diseases above. Granted, those diseases

often progress to a harmful stage, but they need not do so, and some, like carcinoids and indolent prostate cancer, typically do not. And it would be ridiculous to suggest that skin diseases listed as such by physicians writing for physicians, in textbooks of a medical specialty published by medical publishers, are not viewed as truly medical diseases, but only biological ones. Wakefield could, of course, bite the bullet and declare the specialty of dermatology conceptually confused. He could say that dermatologists are wrong to call our five conditions diseases. Perhaps they have misunderstood the general medical concept of disorder and tricked the World Health Organization into doing the same. But since, as we saw, similar examples abound in the subclinical diseases of other medical specialties, it will not be dermatologists alone who are charged with confusion, but doctors quite generally. That is a bridge too far.[33]

Wakefield is unimpressed by these examples or the many others like them. On the contrary: the last one, cherry hemangioma, is one of his own new examples of harmless dysfunctions that are nondisorders. He writes:

> I have a little red dot on my abdomen. Technically, it is a benign angioma. It is known that it is due to a dysfunction in the mechanisms that cause capillaries to smoothly connect to each other during development, so that this particular capillary grew in another direction and connected with the skin instead. Despite its ominous classification as a neoplasm due to the abnormal cell growth, it is entirely harmless both physically and, because it is on a part of my body that is almost always covered, socially and aesthetically as well. Consequently, no one would seriously consider it a medical disorder; it is a harmless anomaly. My benign angioma is a clear case of a harmless dysfunction that is not a medical disorder. (2021b, 519)

These claims are the opposite of the truth about medical usage. First, no medical source would hesitate to classify Wakefield's angioma as a kind of skin pathology. But he has said from the beginning that he uses "disorder" to cover "every pathological condition" (Wakefield, 1992b, 234), since it is "the generic medical term of art for all medical conditions, including diseases and traumatic injuries" (Wakefield, 2000, 20). Thus, if his angioma is pathological, there is no reason, nor has he offered any, not to call it a disorder, indeed a disease. On the contrary, many reference books in dermatology, like Levine (2007) and Gawkrodger (2008), use "disease" as a general heading for all the conditions they describe, including cherry angioma. Such books also often use the term in describing specific conditions, as when Lookingbill and Marks say that "Tinea versicolor is a common disease" (1993, 204), or du Vivier refers to that condition as "the disease" (1993, 13.6). In ICD-10, as I said, cherry angioma, like all my five examples, is in a section with "Diseases" in its title.

Finally, there is no reason, nor has Wakefield offered any, to regard "disorder" as a narrower category than "disease." If anything, it is a broader one, as he said in my quotations above. In the present context, "disease" and "disorder" are merely stylistic variants. Accordingly, other dermatology reference books use "disorder" rather than "disease" as their general term for the conditions they list. Thus, du Vivier (1993) classifies tinea versicolor and tinea pedis under "Superficial fungal disorders of the skin," while common warts are among "Viral disorders of the skin." Everything Wakefield says about his angioma would be equally true of a tiny non-itching wart in the same location, here explicitly called a disorder. As for hemangiomas, they appear in both *Common Skin Disorders* (Epstein, 2001, 115) and *The Encyclopedia of Skin and Skin Disorders*—note the titles—and the latter calls cherry angiomas "harmless" (Turkington and Dover, 2007, 75). Cherry angiomas are also the first entry under "Minor structural vascular disorders" in *Skin Disease in Old Age* (Marks, 1999, 260).[34]

Wakefield's use of the angioma example fits a pattern in his writing. First, he proposes examples that he claims are harmless dysfunctions that are not medical disorders. Next, someone notes—as I did in 2011 (Boorse, 2011) for Wakefield's original examples of albinism, fused toes, and dextrocardia, and in 2015 for cherry angioma—that ICD-10 and other medical references not only list his examples, but call some of them diseases, disorders, or both.[35] Wakefield then dismisses these sources as not meaning what they say, offering excuses for why they say it anyway. This allows him to reaffirm all his examples (Wakefield, 2021b).

His latest effort to defend his original three examples is as follows:

> [S]ome conditions are listed within disorder categories of *ICD-10* because of the need for codes for reimbursement due to associated conditions even when the specific condition itself is clearly a

> non-disorder. For example, the *ICD-10*'s "O-codes" in chapter XV include disorders related to "pregnancy, childbirth, and the puerperium" but also include such nondisordered conditions as "O80. Single spontaneous delivery" that explicitly states that it "includes delivery in a completely normal case," as well as . . . "O04.9. Medical abortion, complete without complication." All of my examples of harmless dysfunctions have complicated versions in which medical intervention is necessary, justifying the codes. (Wakefield, 2021b, 517)

This excuse is hopeless. For one thing, it could only apply to ICD-10, not to standard textbooks and medical reference works not used in coding. In the second place, Wakefield's explanation makes no sense; if anything, it proves the opposite. O-codes, whose section title does not include "disease," show that the ICD-10 writers were quite able to distinguish genuine diseases from normal conditions sometimes complicated by pathology. If they did that in one case (pregnancy, childbirth, and the puerperium), the fact that they did not do it in another—placing, for example, cherry angiomas instead in a category called "diseases"—is evidence that they meant that title "seriously." This example well illustrates how Wakefield treats his intuitions about what is a disorder, even about what medical science views as a disorder, as infallible. Despite his frequent Popperian references to semantic hypotheses, bold predictions, and decisive refutations, his own intuitions are, in the end, immune to evidence. Facing whole classes of harmless disorders so described by standard medical sources, Wakefield, like Harry Potter, just magically waves them out of existence.

VI. CONCLUSION

We began by evaluating Wakefield's criticisms of the BST. His two parallel distinctions, I said, have no place in medical thought—neither a supposed difference between merely biological and medical pathology, nor any notion of disease of an organism's part leaving the whole organism in perfect health. Rather, the medical classification is full of chronic diseases, such as atherosclerosis or emphysema, which are subclinical during most of their course. Some of them, contrary to the HDA's harm criterion, are usually harmless, as with carcinoids and indolent prostate cancer, while skin lesions from warts to angiomas are often harmless even though clinically evident. Of Wakefield's proposed counterexamples to the BST, we saw that one (SIT) involves no dysfunction, while others (missing kidney, asymptomatic infections) are dysfunctions that are indeed viewed as pathological. At worst, the BST is vague about the pathological status of some trivial infections.

As for Wakefield's own added harm criterion, it is, as I noted, directly supported by only two of his 2014 examples (missing kidney and homosexuality). If one analyzes his newly clarified harm test (Wakefield and Conrad, 2019, 2020) in detail, one can argue that although it survives cultural-variation objections if he deletes from it all reference to social values, two other fatal defects remain. First, as we saw, Wakefield must reject the idea of subclinical disease, basic to scientific medicine. Second, although biologists freely apply the health concept to nonsentient organisms, no harm can afflict them separate from dysfunction itself. And for homosexuality, it turns out that the HDA does not, in fact, help psychiatry dodge the dysfunction issue, either by Spitzer's argument or by Wakefield's new version of the harm test. But these are topics for another paper (Boorse, forthcoming).

Given our points above, one can imagine two options for Wakefield. One is to drop the harm criterion entirely, in which case the HDA becomes the BST with a different view of function, based on past selected effects rather than present contributions to fitness. The other option is to admit that his target concept is not *disorder* or *disease* or *pathological condition* at all, but a narrower one. One possibility might be *illness*, except that it is far too narrow: conditions like blindness or paraplegia are serious harmful dysfunctions that do not make one ill. Another possibility would be simply *harmful disorder*, one of the many "disease-plus" notions I mentioned in 1997:

> [T]he BST offers the best of both analytic worlds. It provides a theoretical, value-free concept of disease or pathological condition. But on this foundation one can build value-laden disease concepts, by adding evaluative criteria, to taste. Starting from the basic disease concept, one can define clinically evident disease, or *harmful disease*, or serious disease, or treatable disease, or disabling disease, or disease that should be covered by insurance, or disease that should remove civil or criminal

> responsibility, and so on. Best of all, one can use different "disease-plus" concepts for different purposes. Yet the value-free scientific disease concept remains as a bedrock requirement to block the subversion of medicine by political rhetoric or normative eccentricity. (Boorse, 1997, 100, italics added)

Actually, though, there is no reason why disease-plus concepts must be fact-value hybrids. Instead one could add a second factual conjunct—such as *gross-output* dysfunction.[36] Undoubtedly, medicine recognizes dysfunction occurring at various levels in the organism's physiology, from cell to tissue to organ to organ system to gross output. About such *levels of disease* there is no dispute. My criticism was of the false thesis that, to medicine, lower levels of dysfunction are not health defects of the organism at all, and hence are counterexamples to the BST. On this line, Wakefield would have no need to deny subclinical disease. And if he replaced the harm test with a gross-output test, he could bring the HDA and BST into near-perfect harmony as close linguistic variants of one another. He would merely have to grant that he means "disorder" stipulatively, as *gross dysfunction*, not as it is actually used in medicine. Even clearer, perhaps, would be to use a nontechnical lay term like "malady" (Clouser, Culver and Gert, 1981, 1997) or "ailment."

But Wakefield explicitly rejects a stipulative view of his HDA, and rightly so. Regarding my suggestion that evolutionary biologists tacitly use "the function" to mean "the evolutionary function," he writes: "Of course, one can always stipulate a meaning of a term. However, this dispute is about the conceptual analysis of an existing meaning, not the possibility of stipulating a deviant meaning" (Wakefield, 2021a, 227).[37] Such deviant meanings are inevitably confusing, even when the stipulation is overt and clear. And we may recall Reznek's remark on Szasz:

> If Szasz persists in arguing that it is part of the meaning of disease that there can only be bodily diseases, he is operating with a different concept of disease. He is free to do so, but he will not be speaking the same language as the rest of us. All he will be saying is that mental illnesses are not szasziseases, and there is nothing controversial about this! Anybody is free to invent their own language with special meanings for their terms. (1991, 73)

Worst of all, a stipulative analysis would block Wakefield's overarching aim: to use the HDA to legitimize the DSM, and thereby contemporary psychiatry, by rebutting critics like Szasz. To be sure, Wakefield himself, to his great credit, has been one of DSM's severest and most penetrating critics, especially for the failure of its purely symptomatic diagnostic categories to distinguish mental dysfunction from normal problems in living (1992b, 1997; Wakefield and Horwitz, 2007; Horwitz and Wakefield, 2012). He recognizes that a classification based on dysfunction can never be atheoretic, since the psychological analogue to physiology is a substantive theory of mental functions (Wakefield 1992b, 1997). Nevertheless, he retains a stubborn faith that DSM needs reform, not revolution, and that Spitzer, who led the DSM-III task force, deserves honor as "the leading psychiatric nosologist of our time" (Wakefield 2014, 676). An alternate view is that Spitzer, more than any other person, destroyed the scientific status of psychiatry, in three distinct ways: by saddling psychiatry with a novel unmedical concept of disorder; by insisting on atheoretic and symptom-based classification; and by his silly antipsychological dream of a nosology in which each mental disorder matches some specific chemical imbalance in the brain (Reznek, 2016, 103–104). In reality, atheoretic classifications have never been of much value in the history of medicine. Still, Wakefield views the DSM as conceptually legitimate, insofar as it shares its basic concept—harmful dysfunction—with ordinary medicine.

Unfortunately, our examples above, of subclinical diseases and harmless skin disorders, show that Wakefield's strategy fails, for a reason independent of both usage and his two alleged distinctions. Our examples prove that the HDA does not fit medicine: the ordinary medical classification does not consist only of harmful dysfunctions, or even of gross-output dysfunctions. But if the HDA does not fit medicine, then if the HDA fits the DSM, the DSM does not fit medicine. This basic mismatch remains regardless of how anyone uses terms like "disorder," "disease," and "pathological condition,"[38] and regardless of Wakefield's two distinctions. In the end, then, what our examples show is a gulf between the HDA and contemporary psychiatry, on the one hand, and scientific medicine and the BST on the other.

NOTES

1 See Wakefield (2014, 2020, 2021a, 2021b). To be sure, Wakefield disagrees with me not merely over the need for a harm clause in defining disorder, but also over the analysis of biological function. He called his 2014 paper "part 1" of a two-part critique, with the second part to deal with function, and he has now contrasted our two function theories at length (Wakefield 2021a). In this paper, I answer only his critique of the BST for its lack of a harm clause; I will defend my function analysis elsewhere.

2 The guide volume explains:

> The ICD has developed as a practical, rather than a purely theoretical classification, in which there are a number of compromises between classification based on etiology, anatomical site, circumstances of onset, etc. There have also been adjustments to meet the variety of statistical applications for which the ICD is designed, such as mortality, morbidity, social security and other types of health statistics and surveys. (World Health Organization, 1994, vol. 2, 12)

A bit earlier, the guide says: "Although the ICD is suitable for many different applications, it does not always allow the inclusion of sufficient detail for some specialties . . ." (World Health Organization, 1994, 3).

3 I find it ironic that Wakefield (2014) threatens me with Ockham's razor for my view that "disease" is ambiguous between pathological and clinical uses—an ambiguity for which I offer direct linguistic evidence below—yet proposes, on no linguistic evidence at all, that "pathology" is ambiguous between "biological" and "medical" types. In my view, it is he who offers a "postulated conceptual bifurcation" that is "an ad hoc hypothesis formulated to avoid falsification" of his analysis (Wakefield, 2014, 651).

4 Strictly, what is at stake here is only whether part-pathology entails (not "equals") medical disorder.

5 Of course, as with metastatic cancer, it might have originated in another organ, and therefore be called by that organ's name.

6 As far as I know, this distinction was first drawn by Grisez and Boyle (1979), but later repeated and popularized by Culver and Gert (1982). The common idea is that the life of an organism ends when "integrated" or "integrative" functions cease—for example, at whole-brain death—after which (the writers believed) local functions like hair or nail growth may still continue.

7 Since "symptoms," in strict usage, are disease effects noted by the patient, "subclinical" goes beyond "asymptomatic" in requiring also the absence of "signs," or disease effects noted by the physician. Signs include information from physical examinations, laboratory tests, and other diagnostic procedures.

8 Medscape states: "Chronic bacterial prostatitis (CBP) is not associated with mortality."

9 Wikipedia states: "The term *prostatitis* refers, in its strictest sense, to histological (microscopic) inflammation of the tissue of the prostate gland." This strict sense contrasts with various clinical syndromes caused by such inflammation—that is, with what one might call, with no fear of Ockham, "clinical prostatitis" (July 2015). This contrast between strict pathological and loose clinical meanings of a disease term recurs over and over, as shown in the next section.

10 A natural term might be "chronic autoimmune β-insulitis," but I have not seen it used, only the noun "insulitis" (Cotran, Kumar, and Collins, 1999, 916).

11 Terminological confusion is even more evident in the Rubin text's discussion. Its first paragraph reserves "Type 1 diabetes mellitus" for the clinical phase, when there are "few if any functional β cells . . . and extremely limited or nonexistent insulin secretion" (Rubin and Gorstein, 2004, 1174). Later, however, the text uses "T1DM" to refer to the whole process, using such terms as "overt diabetes" and "clinically apparent diabetes" (Rubin and Gorstein, 2004, 1176–1177).

12 Medscape, "Drugs and Disease," "Coronary Artery Atherosclerosis," "Pathophysiology" (July 2015). Unlike many other online medical sources, Medscape is written for physicians and other health professionals to summarize current theory and practice.

13 The Robbins text says: "Fatty streaks appear in the aortas of . . . all children older than 10 years, regardless of geography, race, sex, or environment. Coronary fatty streaks are less common than aortic but begin to form in adolescence . . ." (Cotran, Kumar, and Collins, 1999, 503).

14 Same Medscape (July 2015) article, "Background" section.

15 Medscape admits this when it writes: "The true frequency of atherosclerosis is difficult, if not impossible, to accurately determine because it is a predominantly asymptomatic condition. The process of atherosclerosis begins in childhood with the development of fatty streaks." (Same article, "Epidemiology" section). Note the term "true."

16 On the BST, of course, it is hard to see how a condition affecting most of the human species can be a disease. Accordingly, I suggested in the past that what is pathological is only age-excessive atherosclerosis (Boorse, 1977, 1997). But this does not affect my point here. Since contemporary medical sources both describe all atherosclerosis as a disease from the fatty plaque onward and say that it afflicts nearly all adults, my quotations are good evidence that "CAA" and "CAD" are sometimes given a clinical, not a pathological, sense.

17 "The primary function of the kidneys . . . is usually remarkably well-preserved until late in the course of chronic renal disease (CRD) . . . Nephron hypertrophy and hyperfunction combine to compensate for the acquired renal functional deficits." (Brenner, 2000, 1901).

18 In his first new sentence on p. 673, Wakefield (2014) seems to concede that a missing kidney is a pathological condition. But, for the reason I just gave, it can only be a pathological condition of the individual, not of the organ.

19 Wikipedia, "Semen quality" (July 2015), says that of the "300–500 million" sperm in a young man's semen, "only a couple of hundred survive in the acidic environment of the vagina to be candidates for successful fertilization."

20 That is the answer to Wakefield's remark that my view "confusingly looks for the inferred dysfunction in the *effects* of situs inversus rather than in its *cause*" (2014, 651). If SIT never reduced S&R, whatever causes the standard orientation has no biological function on either my analysis or his own.

21 A recent summary of Mary's case says that there was an autopsy showing that "she shed *S. typhi* bacteria from her gallstones" (Marineli et al., 2013, 133). Soper, however, says that there was no autopsy (1939, 712).

22 A treatise on infectious diseases notes: "Chronic typhoid carriage is more likely in the presence of chronic diseases of the liver (opisthorchiasis), gallbladder (cholelithiasis), or urinary tract . . ." (Cohen and Powderly, 2004, 1565).

23 For a discussion of the legal issues, see ch. 3, "'A Menace to the Community': Law and the Limits of Liberty," in Leavitt (1996). Leavitt says that there was actually "no discussion" of this legal issue (1996, 88). That is partly because Mary's defense denied her carrier status, in part relying on stool samples from a private laboratory that were free of *S. typhi*.

24 The ICD-10 index refers "Ghon tubercle, primary infection" to A16.7 (World Health Organization, 1994, vol. 3, 244). It refers "latent" to the name of the condition, and "tubercular infection without clinical manifestations" to A16.7. Medscape's summary of the Ghon lesion is as follows. (Note the term "symptomatic disease.")

> The typical TB lesion is an epithelioid granuloma with central caseation necrosis. The most common site of the primary lesion is within alveolar macrophages in subpleural regions of the lung. Bacilli proliferate locally and spread through the lymphatics to a hilar node, forming the Ghon complex.
>
> Initial lesions may heal and the infection become latent before symptomatic disease occurs. Smaller tubercles may resolve completely. Fibrosis occurs when hydrolytic enzymes dissolve tubercles and larger lesions are surrounded by a fibrous capsule. Such fibrocaseous nodules usually contain viable mycobacteria and are potential lifelong foci for reactivation or cavitation.

25 Of course, I do not accept the Supreme Court as the final arbiter of medicine, or even of constitutional law. But the *Bragdon* opinion purports to be reporting the best medical information of its time, and is therefore evidence of medical usage.
26 To a physiologist, the mucosa of the gut, lung, and other organs is part of the torus-shaped organism's outer boundary. That is why such tissue is called "epithelium," not "endothelium." So *E. coli* and similar bacteria, like those living on skin, are in the organism's environment. However mucosal cells function in that environment, that is normal function.
27 She goes so far as to say that the "ubiquitous presence" of certain viruses "implies functions" (Roossinck, 2015, 6534). Herbert Virgin's (2014, 142, 144–145) survey also recognizes mutualistic viruses.
28 An exception is Griffiths, who writes:

> [A]ctive infection with a bacterial or viral pathogen does not guarantee that 100% of individuals will contract disease, e.g. nasal carriage of meningococci leads to frank meningitis in only a small proportion of people, and polioviruses cause disease in only 1% of infected cases. (1999, 73)

But his term "frank" supports my view: the carrier state is not "frank" disease, but still disease, and it is not "disease" that 99% of poliovirus infections fail to cause, but only specific clinical syndromes like poliomyelitis. Earlier, Griffiths seemed to imply that viral infection does not necessarily "perturb normal cellular function" (1999, 73). In that case, Griffiths, too, like Wakefield and Conrad's other writers, may be contrasting infection with dysfunction, not dysfunction with disease.
29 Roossinck (2015, 6532): "the line between virus and host is blurred."
30 Earlier, the authors stipulated to use "symptom" to cover signs as well, so what they here reject is precisely subclinical disease (Wakefield and Conrad, 2020, 352).
31 For example, Rogers and Mintzker write: "current medical terminology explicitly accepts the notion of non-harmful disease" (2016, 581). Further references can be found simply by an internet search on "subclinical disease."
32 The ICD-10 index refers "senile angiomas" to I78.1, although "hemangiomas" in general are under D18.0 ("neoplasms").
33 Actually, I made a somewhat similar move myself in excluding from the BST two categories of recognized diseases: purely structural abnormalities and typical diseases (Boorse, 1977, 1997). But I said I felt forced to do so in order to achieve a unified analysis of disease; I could not see how to fit the two "anomalies" into one. Unlike Wakefield, however, I never denied that medicine classifies the conditions as disorders. Here, we need not even attribute any conceptual error to medical sources, since Wakefield concedes that the BST covers examples such as skin disorders and all of the HDA's disorders besides.
34 Despite explicitly calling them a disorder, Marks says "[t]hey seem to have no particular significance and cause no symptoms" (1999, 260). All ten of my dermatology source books are either written or co-written by physicians.
35 For example, albinism in ICD-10 is under "disorders of aromatic amino-acid metabolism," a subcategory of "endocrine, nutritional and metabolic diseases" (World Health Organization, 1994, vol. 1, 297–298). A different approach to albinism is de Block and Sholl's (2021) careful and convincing argument that albinism is in fact harmful.
36 This possibility is also noted by Dussault (2021), who, however, describes the revised clause as requiring dysfunction of the organism, not of its gross output.
37 Citing my (Boorse, 2002, 80). Actually, my suggestion was a stipulated evolutionary meaning not for "function," but for "the."
38 As we have seen, Wakefield's claims about medical usage are false. But if they were true, our examples would merely show that the medical classification does not consist only of disorders, so that if DSM does, then psychiatry does not match medicine.

REFERENCES

Boorse, C. 1976. Wright on functions. *The Philosophical Review* 85(1):70–86.
———. 1977. Health as a theoretical concept. *Philosophy of Science* 44(4):542–73.
———. 1987. Concepts of health. In *Health Care Ethics: An Introduction*, eds. D. VanDeVeer and T. Regan, 359–93. Philadelphia: Temple University Press.
———. 1997. A rebuttal on health. In *What Is Disease?* eds. J. M. Humber and R. F. Almeder, 1–134. Totowa, NJ: Humana Press.
———. 2002. A rebuttal on functions. In *Functions: New Essays in the Philosophy of Psychology and Biology* eds. A. Ariew, R. Cummins, and M. Perlman, 63–112. Oxford, United Kingdom: Oxford University Press.
———. 2010. Disability and medical theory. In *Philosophical Reflections on Disability*, eds. D. C. Ralston and J. Ho, 55–88. Dordrecht, Netherlands: Springer.
———. 2011. Concepts of health and disease. In *Handbook of Philosophy of Science: Philosophy of Medicine*, ed. F. Gifford, 13–64. Oxford, United Kingdom: Elsevier.
———. 2021. Reznek on health. *Teorema* 40(1):23–65.
———. Forthcoming. Wakefield on harm, health, and homosexuality. *Medical Research Archives*.
Brenner, B. M. 2000. *Brenner and Rector's The Kidney*. 6th ed. Philadelphia: Saunders.
Centers for Disease Control and Prevention. 2021. *Principles of Epidemiology in Public Health Practice*. 3rd ed. Washington, DC: CDC.
Clouser, K. D., C. M. Culver, and B. Gert. 1981. Malady: A new treatment of disease. *The Hastings Center Report* 11(3):29–37.
———. 1997. Malady. In *What Is Disease?* eds. J. M. Humber and R. F. Almeder, 173–217. Totowa, NJ: Humana Press.
Cohen, J., and W. G. Powderly, eds. 2004. *Infectious Diseases*. 2nd ed. Edinburgh, United Kingdom: Mosby.
Cotran, R. S., V. Kumar, and T. Collins. 1999. *Robbins Pathologic Basis of Disease*. 6th ed. Philadelphia: W. B. Saunders.
Culver, C. M., and Gert, B. 1982. *Philosophy in Medicine*. New York: Oxford University Press.
de Block, A., and J. Sholl. 2021. Harmless dysfunctions and the problem of normal variation. In *Defining Mental Disorder: Jerome Wakefield and His Critics*, eds. L. Faucher and D. Forest, 495–510. Cambridge, MA: The MIT Press.
du Vivier, A. 1993. *Atlas of Clinical Dermatology*. 2nd ed. London, United Kingdom: Gower Medical Publishing.

Dussault, A. C. 2021. Wakefield's harmful dysfunction analysis of disorder and the problem of defining harm to nonsentient organisms. *Theoretical Medicine and Bioethics* 42(December):211–31.
Epstein, E. 2001. *Common Skin Disorders*. 5th ed. Philadelphia: W. B. Saunders.
Fitzpatrick, T. B., R. A. Johnson, K. Wolff, M. K. Polano, and D. Suurmond. 1992. *Color Atlas and Synopsis of Clinical Dermatology*. New York: McGraw-Hill.
Freedberg, I. M., A. Z. Eisen, K. Wolff, K. F. Austen, L. A. Goldsmith, S. I. Katz, and T. Fitzpatrick, eds. 1999. *Fitzpatrick's Dermatology in General Medicine*. 5th ed. New York: McGraw-Hill.
Fundukian, L. J., ed. 2011. *Gale Encyclopedia of Medicine*. 2nd ed. Detroit: Gale.
Gawkrodger, D. 2008. *Dermatology*. 4th ed. New York: Elsevier.
Griffiths, P. 1999. Time to consider the concept of a commensal virus? *Reviews in Medical Virology* 9(2):73–4.
Grisez, G., and J. M. Boyle. 1979. *Life and Death with Liberty and Justice*. Notre Dame, IN: University of Notre Dame Press.
Hall, J. C. 2000. *Sauer's Manual of Skin Diseases*. 8th ed. Philadelphia: Lippincott Williams and Wilkins.
Harrison, T. R., and G. W. Thorn, eds. 1977. *Harrison's Principles of Internal Medicine*. 8th ed. New York: McGraw-Hill.
Horwitz, A. V., and J. C. Wakefield. 2012. *All We Have to Fear*. New York: Oxford University Press.
Kendell, R. E. 1975. The concept of disease and its implications for psychiatry. *The British Journal of Psychiatry: The Journal of Mental Science* 127(4):305–15.
Leavitt, J. W. 1996. *Typhoid Mary: Captive to the Public's Health*. Boston: Beacon Press.
Levine, N. 2007. *Dermatology: Diseases and Therapy*. New York: Cambridge University Press.
Lookingbill, D. P., and J. G. Marks, Jr. 1993. *Principles of Dermatology*. 2nd ed. Philadelphia: W. B. Saunders.
Mandell, G. L., J. E. Bennett, R. Dolin, and R. G. Douglas. 2000. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Disease*. Philadelphia: Churchill Livingstone.
Marineli, F., G. Tsoucalis, M. Karamanon, and G. Androvitsos. 2013. Mary Mallon (1869–1938) and the history of typhoid fever. *Annals of Gastroenterology* 26(2):132–4.
Marks, R. 1999. *Skin Disease in Old Age*. 2nd ed. London, United Kingdom: Martin Dunitz.
McVeigh, E., R. Hamburg, and J. Guillebood, eds. 2008. *Oxford Handbook of Reproductive Medicine and Family Planning*. New York: Oxford University Press.
Nordenfelt, L. 1987. *On the Nature of Health*. Dordrecht, Netherlands: Reidel.
Porter, R. S., ed. 2011. *The Merck Manual*. Whitehouse Station, NJ: Merck.
Reznek, L. 1991. *The Philosophical Defense of Psychiatry*. London, United Kingdom: Routledge.
———2016. *Peddling Mental Disorder: The Crisis in Modern Psychiatry*. Jefferson, NC: McFarland.
Rogers, W. A., and Y. Mintzker. 2016. Getting clearer on overdiagnosis. *Journal of Evaluation in Clinical Practice* 22(4):580–7.
Rogers, W. A., and M. J. Walker. 2017. The line-drawing problem in disease definition. *The Journal of Medicine and Philosophy* 42(4):405–23.
Roossinck, M. J. 2011. The good viruses: Viral mutualistic symbioses. *Nature Reviews Microbiology* 9(2):99–108.
———. 2015. Move over, bacteria! Viruses make their mark as mutualistic microbial symbionts. *Journal of Virology* 89(13):6532–5.
Rubin, E., and F. Gorstein, eds. 2004. *Rubin's Pathology: Clinicopathologic Foundations of Medicine*. 4th ed. Philadelphia: Lippincott Williams and Wilkins.
Soper, G. A. 1939. The curious career of Typhoid Mary. *Bulletin of the New York Academy of Medicine* 15(10):698–712.
Tannock, G. W. 1999. *Medical Importance of the Normal Microflora*. Dordrecht, Netherlands: Kluwer Academic Publishers.
Turkington, C., and J. S. Dover, eds. 2007. *The Encyclopedia of Skin and Skin Disorders*. 3rd ed. New York: Facts on File.
Virgin, H. W. 2014. The virome in mammalian physiology and disease. *Cell* 157(1):142–50.
Virgin, H. W., E. J. Wherry, and R. Ahmed. 2009. Redefining chronic viral infection. *Cell* 138(1):30–50.
Vu, D. L., and L. Kaiser. 2017. The concept of commensal viruses almost 20 years later: Redefining borders in clinical virology. *Clinical Microbiology and Infection* 23(10):688–90.
Wakefield, J. C. 1992a. The concept of mental disorder: On the boundary between biological facts and social values. *The American Psychologist* 47(3):373–88.
———. 1992b. Disorder as harmful dysfunction: A conceptual critique of DSM-III-R's definition of mental disorder. *Psychological Review* 99(2):232–47.
———. 1997. Diagnosing DSM-IV, part 1: DSM-IV and the concept of mental disorder. *Behaviour Research and Therapy* 35(7):633–49.
———. 1999. Mental disorder as a black box essentialist concept. *Journal of Abnormal Psychology* 108(3):465–72.
———. 2000. Aristotle as sociobiologist: The 'function of a human being' argument, black box essentialism and the concept of mental disorder. *Philosophy, Psychiatry, Psychology* 7(1):17–44.
———. 2013. Addiction, the concept of disorder, and pathways to harm: Comment on Levy. *Frontiers in Psychiatry* 4(May):1–2.
———. 2014. The biostatistical theory versus the harmful dysfunction analysis, part 1: Is part-dysfunction a sufficient condition for medical disorder? *Journal of Medicine and Philosophy* 39(6):648–82.

———. 2021a. Is the harmful dysfunction analysis descriptive or stipulative, and is the HDA or BST the better naturalist account of dysfunction: Reply to Mael Lemoine. In *Defining Mental Disorder: Jerome Wakefield and His Critics*, eds. L. Faucher and D. Forest, 213–49. Cambridge, MA: The MIT Press.

———. 2021b. Can the harmful dysfunction analysis distinguish problematic normal variation from disorder? Reply to Andreas De Block and Jonathan Sholl. In *Defining Mental Disorder: Jerome Wakefield and His Critics*, eds. L. Faucher and D. Forest, 511–36. Cambridge, MA: The MIT Press.

———. 2021c. Must social values play a role in the harm component of the harmful dysfunction analysis? Reply to Rachel Cooper. In *Defining Mental Disorder: Jerome Wakefield and His Critics*, eds. L. Faucher and D. Forest, 553–75. Cambridge, MA: The MIT Press.

Wakefield, J. C., and J. A. Conrad. 2019. Does the harm component of the harmful dysfunction analysis need rethinking? Reply to Powell and Scarffe. *Journal of Medical Ethics* 45(9):594–6.

———. 2020. Harm as a necessary component of the concept of medical disorder: Reply to Muckler and Taylor. *Journal of Medicine and Philosophy* 45(3):350–70.

Wakefield, J. C., and A. V. Horwitz. 2007. *The Loss of Sadness*. New York: Oxford University Press.

World Health Organization. 1994. *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision [ICD-10]*. Geneva, Switzerland: WHO.

World Health Organization. 2006. *Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia*. Geneva, Switzerland: WHO.